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THE EARLY DIAGNOSIS AND RADICAL CURE OF CARCINOMA OF THE PROSTATE.

BEING A STUDY OF 40 CASES AND PRESENTATION OF A RADICAL OPERATION WHICH WAS CARRIED OUT IN FOUR CASES.

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The recent publication of Courvoisier, Wolff, Socin and Burckhardt, and Albarran and Hallé, have furnished a considerable stimulus to the study of cancer of the prostate, but although the disease has been shown to be much more frequent than was formerly supposed, and the pathological aspects have been well elucidated, practically nothing has been suggested in recent years as a routine operation for its radical cure.

Albarran's startling announcement that in 100 specimens of supposed benign hypertrophy he found more or less pronounced invasion of carcinoma in 14, seems not to have suggested the necessity of a radical excision, and even at this late date we find Pousson and Hawley advocating a mere enucleating prostatectomy, leaving behind the prostatic capsule, urethra, anterior commissure, the adjacent vesical mucosa and the seminal vesicles—structures which are manifestly in intimate contact with cancerous lobes.

The need of early diagnosis and radical methods of removal has been brought forcibly to the writer's attention in the past two years by the sad results arising from his failure to recognize, and to operate radically in six cases of early carcinoma of the prostate—several of which ought certainly to have been cured by the operation which he has since carried out in four cases. The object of this paper is to give in detail:

I. The six cases of early carcinoma in which the malignant nature of the disease was not recognized and a partial operation performed.

II. A radical operation, proposed as a routine for cases of cancer of the prostate, with histories of four operated cases.

III. A clinical and pathological study of 40 cases of carcinoma of the prostate.

IV. A comparison with cases in the literature in which operations for carcinoma of the prostate were performed.

V. Conclusions as to the practicability of early diagnosis and the radical cure of the disease.

I. Cases of Unrecognized Early Carcinoma with Partial Operation.

Case I. Male, aged 67. Admitted May 9, 1901. Duration of symptoms 2 years and 4 months. Uses a catheter, has had no hematuria and very little pain. Prostate much enlarged in left lateral lobe which is soft. Right lateral lobe not enlarged but indurated. Cystoscope shows enlargement of left lateral lobe and a small median bar. Diagnosis: benign prostatic hypertrophy. Bottini operation. Excellent result;

maintained for 2½ years. Returned three years after operation complaining of pain in bladder and urethra, frequent urination. Prostate much enlarged and indurated in both lateral lobes; seminal vesicles also involved. Cystoscope showed large irregular villous outgrowth in region of left lateral lobe which involved also the bladder. Death three months later. Autopsy showed the bladder invaded almost everywhere by malignant neoplasm, involving also the prostate. Microscope shows carcinoma.

Case II. E. G. W., aged 67. Admitted November, 1901. Difficulty of urination 2½ years duration. Catheterism for one year. Severe pain in bladder of late. Prostate considerably enlarged, smooth but very hard. Seminal vesicles not indurated. Residual urine 70 cc. Cystoscope shows large irregular calculus. Slight enlargement of lateral and median portions of prostate. Operation. Suprapubic lithotomy and complete prostatectomy. Recovery. Cure, maintained for 3 years and 10 months. Six months ago began to have pain in region of left kidney. Can now hold his urine for 5 hours, voids easily, no residual urine, bladder large, no pain in that region. Examination shows a large irregular mass beneath the left kidney. Liver enlarged and nodular. In region of prostate a very hard irregular mass. Cystoscope shows no intravesical obstruction or enlargement. Examination of specimen removed at first operation shows carcinoma of the prostate.

Case III. W. H., aged 56 years. Admitted May, 1902. Duration of symptoms two years. Now voids urine 30 times a day. No hematuria, no pain on urination, but severe pain is present in the region of the sacrum. Prostate enlarged and indurated in both lateral lobes. Left seminal vesicle also indurated. Cystoscope shows very little intravesical enlargement of prostate. Bottini operation. Five months later patient reported he had no difficulty in urination, but had pain in his spine and down his legs; this gradually grew worse and patient died six months later, evidently from carcinoma of prostate.

Case IV.—J. S., aged 68 years. Admitted August, 1902. Frequency and difficulty of urination for two years. Very little pain—no hematuria. Prostate much enlarged, large indurated nodule at upper end of each lobe. Residual urine 450 cc. Bottini operation, with good results for 20 months. Then return of difficulty; had to use a catheter. December, 1904; cannot void naturally, uses a catheter, has no pain. General glandular enlargement present. Prostate and seminal vesicles involved in a large irregular indurated mass. Cystoscope shows intravesical tumor.

Case V.—A. F., aged 60 years. Admitted September, 1902. Frequency of urination for three years. No pain, no hematuria. Prostate enlarged and indurated in both lobes. Left seminal vesicle also indurated. Cystoscope shows a slight hypertrophy of median and lateral lobes. Bottini operation. Excellent result maintained until January, 1904. After that difficulty and frequency of urination, pain and hematuria. Examination April, 1904. Prostate very large hard, nodular. Seminal vesicles involved on both sides. Cystoscope shows considerable outgrowth into the bladder. Patient died 8 months later.

Case VI.—J. J. S., aged 75. Admitted September 18, 1903. Frequency and difficulty of urination for three years. Pain in bladder, perineum and urethra—no hematuria. Uses catheter 6 times a day. Prostate considerably enlarged, very hard, slightly irregular, not tender. Seminal vesicles not palpable. Cystoscopic examination shows slight intravesical enlargement of prostate. Perineal prostatectomy, enucleation difficult owing to induration and adhesions. Immediate result good, and maintained for 9 months. Examination 10 months after operation. Difficulty of urination has returned. Residual urine 500 cc. Large irregular indurated mass involving prostate and seminal vesicle. Cystoscope showed marked increase in intravesical enlargement. Bottini operation. Improved. Death two months later. Tissue removed at prostatectomy showed adenocarcinoma.

Remarks.—In none of the foregoing six cases were the classical symptoms of prostatic carcinoma, as usually given, present. Pain was present only in the case with calculus and none had hematuria. The clinical picture of nearly all of the cases was that of the so-called sclerotic prostatic hypertrophy. Induration was a common finding in all the cases and the cystoscope showed very little intravesical hypertrophy. The failure to recognize the malignant nature of the enlargement in these cases caused the writer to be more careful, and to be suspicious of marked induration associated with little intravesical hypertrophy.

II. Four Cases of Carcinoma of the Prostate Recognized Early and Operated upon Radically.

In March, 1904, patient aged 70, who had suffered from frequency and difficulty of urination for one year, which had been unimproved by a Bottini operation three months before, presented himself. The prostate was hard, slightly nodular, induration extending into the region of the left seminal vesicle. The cystoscope showed only a slight intravesical prostatic enlargement. Pain had been slight and hematuria absent, but diagnosis of carcinoma was made because of the induration, and absence of intravesical enlargement. The patient gave his consent to a radical operation and the entire prostate, with the urethra and capsule, a cuff of an adjacent portion of the bladder including most of the trigone and the seminal vesicles, was removed in one piece. The operation was performed as follows with the kind assistance of Dr. Halsted:

An inverted V cutaneous incision was made in the perineum as in the operation employed by me for simple hypertrophy of the prostate—each branch of the incision being about two inches long. By blunt dissection the end of the bulb and central tendon were exposed, and the latter divided, exposing in turn the recto-urethralis muscle, the division of which gave free access to the membranous urethra behind the triangular ligament. Urethrotomy upon a grooved staff, was followed by introduction of the prostatic tractor, which was opened out

after it reached the bladder. While traction was made upon this instrument the rectum was carefully separated from the prostatic capsule by blunt dissection until the entire posterior surface of the prostate was brought into view. Up to this point the operator proceeded exactly as in the usual prostatectomy operation with the exception that the tissues around the prostate were more hemorrhagic and the wall of the rectum more closely adherent to the capsule of the prostate than usual. Examination of the prostate then showed much greater induration than I have ever encountered in the benign prostate. The rectum and periprostatic tissues were free from invasion. Complete excision was therefore decided upon, and carried out as follows: The handle of the tractor was depressed, thus exposing the membranous urethra anterior to it at a point where it was easily divided transversely with a scalpel, leaving a small stump of the membranous urethra protruding from the surface of the triangular ligament. By further depressing the handle of the tractor the pubo-prostatic ligament was exposed, and being very tautly drawn, easily divided by scissors, thus completely severing the prostate from all important attachments (except posteriorly) as shown in Fig. 1. The lateral attachments, which are slight, were easily separated by the finger. During these manipulations a moderate amount of hemorrhage was encountered (coming from the prostatic veins, particularly those just behind the triangular ligament in front of the prostate) but it was easily controlled by clamping several bleeding points, and applying pressure with gauze by means of an anterior deep retractor (see Fig. 3).

The posterior surface of the seminal vesicles were then freed by blunt dissection, the now mobile prostate being well out of the wound, as shown in Fig. 2. In this exposure of the posterior surface of the vesicles I was careful not to break through the fascia of Denonvilliers which covers not only the posterior surface of the prostate but also of the seminal vesicles, and forms I believe an important barrier to the backward growth of the disease.

The next step was to expose the anterior surface of the bladder, which was easily done by depressing the tractor and making strong traction. By this procedure, the bladder was drawn down so close to the skin wound that it was easily incised at a point in the middle line about 1 cm. behind the prostatovesical juncture, as shown in Fig. 3.

By means of scissors the division was continued on each side until the trigone was exposed, Fig. 4. After swabbing away the blood and urine the ureters were easily found and the line of incision carried across the trigone with a scalpel so as to pass about 1 cm. in front of the ureteral orifices.

While still making traction upon the prostate, the base of the bladder was pushed upward with the handle of the scalpel, thus exposing the anterior surface of the seminal vesicles and the adjacent vasa deferentia, Fig. 5, all of which were carefully freed by blunt dissection with the finger as high up as possible, so as to remove with the vesicles much circumjacent fat and areolar tissues on account of the lymphatics which they contained. The vasa deferentia after being drawn well down were picked up on a small blunt hook and divided with scissors as high up as possible, care being taken to see that the ureters were not in danger. After division of the vasa, the seminal vesicles were found to come down more readily, the deep adhesions were finally divided and the mass shown in the photograph, Fig. 6, was removed. As seen here in the side view, a portion of the membranous urethra, the entire prostate with its capsule intact, the seminal vesicles, 4 cm. of the vasa deferentia, and a cuff of the bladder 1 cm. wide along the anterior and lateral surfaces and 2 cm. wide in the region of the trigone has been removed in one piece. Fig. 7 shows the posterior view of the tissues removed.

There now remained a large defect to be repaired. The vesicle opening was about 8 cm. in diameter and had sunk far back into the depths. The stump of the membranous urethra had been obliterated by the compression of the anterior retractor so that it was necessary to insert a soft rubber catheter through the urethra from the meatus to discover it. The anterior wall of the vesicle opening was then caught with forceps, and with no great traction I was surprised to find how easily it could be drawn down to the membranous urethra, where an anastomosis was readily made as shown in Fig. 8. The first suture was placed by inserting the needle into the triangular ligament above the urethra and out through the anterior wall of the membranous urethra, then through the anterior wall of the bladder in the median line, from within out, care being taken to include only the submucosa and muscle. When this suture was tied, the median line of the anterior wall of the bladder was drawn to meet the median line of the roof of the remaining membranous urethra, the knot outside, and the thread left long.

Lateral sutures, similarly placed (including the periurethral muscular structures below), and two posterior sutures completed the anastomosis of the membranous urethra with a small ring into which the anterior portion of the margin of the vesical wound had been fashioned by the tying of the sutures, as shown in Fig. 8. The remainder of the vesical wound now presented as a longitudinal opening which was easily closed by sutures, placed as shown in Fig. 8, thus completely closing the defect and replacing the prostatic urethra with a funnel-shaped process made from the bladder wall. The sutures used were silk, one end of each being left long and brought out of the wound so that they could be extracted later (since then I have found alternate sutures of catgut and silk-worm gut, also left long, the best). After light gauze packing had been placed in various portions of the wound, the levator ani muscles were drawn together with catgut (two sutures) in front of the rectum and the skin wound closed on each side with interrupted catgut sutures leaving only a small portion open at the angle in front for exit of the gauze drainage. The rubber catheter (which was of considerable service in making the anastomosis of the urethra and bladder) was fastened in place, by adhesive plaster around the penis, and the patient was returned to the ward. During the operation he received 1000 cc. salt solution

infusion beneath the breast, and his condition throughout was good, pulse varying from 65 to 92, and 80 at the end of the operation which required two hours.

A study of the specimen removed showed adenocarcinoma involving the entire prostate, the region between the seminal vesicles and the inferior surface of the excised trigone and the vasa deferentia. The capsule of the prostate and the bladder at upper limit of excision were free, but along the left vas deferens the disease extended to the upper limit of the incision 4 cm. above the prostate.

Convalescence.—Patient convalesced well. Left the hospital May 30, 1904. Perineal wound healed tight; no difficulty in urination; able to hold his urine for three or four hours at night; incontinence in the day.

December 22, 1904. Condition of patient excellent until 2 months ago when he began to suffer pain in the urethra. Examination shows three calculi in the bladder. Operation, litholapaxy. One calculus was found attached to a silk ligature and in removing this the mucous membrane of the bladder was torn. This was followed by perineal abscess, extravasation of urine and death four weeks later. Autopsy showed excellent union between bladder and urethra. No recurrence in bladder, but behind bladder along left vas deferens was a small area of carcinoma. No carcinomatous glands present.

Case VIII.—W. R., No. 16,675. Admitted September 14, 1904, aged 64. Frequency and difficulty of urination for three years. Has to use catheter now. No hematuria, no pain. Prostate moderately enlarged, smooth, very hard but not nodular. Between the two seminal vesicles an indurated plateau continuous with the prostate below. No indurated glands or lymphatics. Cystoscope showed slight intravesical enlargement of median portion. Diagnosis: carcinoma of the prostate. Operation September 23, 1904. Total excision of prostate, seminal vesicles, portion of the vasa deferentia, cuff of the bladder, the entire trigone including the ureteral orifices. The excision was carried above the ureteral orifices because the bladder wall there felt indurated and the operator thought it was involved. Examination of the tissue removed, however, showed that this was a mistake, and that only the anterior part of the trigone was invaded by the disease. Transplantation of the ureters was not necessary because the intramural portion had not been completely removed. Anastomosis of anterior wall of bladder and urethra was made as in case VII. The patient convalesced badly, early showed symptoms of pyelitis and died November 8, 1904.

Autopsy showed ascending infection of both kidneys and besides that chronic endocarditis, perihepatitis, splenitis, pancreatitis. Careful examination showed that the carcinoma had been entirely removed at operation. No metastatic glands present. The patient would almost certainly have been cured had the operator not excised the ureteral papillæ.

Case IX.—S. R. B., aged 65. Admitted February 4, 1905. Frequency and difficulty of urination for four years. Now voids every few minutes. Intermittent pain in left hip and thigh for two years. Dull pain in back, bladder, perineum, and rectum. Has never had hematuria. Examination: No glandular enlargements. Prostate considerably enlarged, smooth but very hard. Induration involving the lower end of the seminal vesicle on each side with a narrow plateau between them above the prostate. Cystoscope shows very slight enlargement of the median portion of the prostate. Diagnosis of carcinoma of the prostate made upon the induration involving also the seminal vesicles and the area between them, and the absence of intravesical prostatic enlargement.

February 16, 1905. Radical operation was carried out as in case VII. Patient made an excellent recovery. Was entirely relieved of pain. Perineal wound healed tight. Urine comes entirely through the urethra.

Examination June 24. Condition excellent. Voids urine about every 2 hours. Has no incontinence at night, but in the day urination is imperative when desire comes on. Examination shows no evidence of recurrence.

Study of the tissue removed at operation shows adenocarcinoma involving the prostate, both seminal vesicles, vasa deferentia and the tissues between them and the excised portions of the bladder.

Case X.—J. E. D., aged 64. Admitted May 12, 1905. Difficulty and frequency of urination for one year. For two months has had to use a catheter. No pain in region of bladder, rectum, back or legs. Has not lost weight. No hematuria. Healthy looking man. No glandular enlargement. Prostate considerably enlarged, particularly left lateral lobe which is very hard and tender. The seminal vesicle is indurated on this side. Residual urine about 400 cc. Cystoscope shows small enlargement of the median portion of the prostate. Diagnosis of carcinoma made on induration, extending into the region of the seminal vesicle and the absence of marked intravesical enlargement.

May 16, 1905. Radical operation carried out as in Case VII. The patient made an excellent convalescence. Perineal wound healed in 5 weeks. Discharged from hospital in six weeks. General condition excellent. Suffers no pain, urine passes entirely through the urethra. Rectal examination negative. Patient feels well, but as yet has no control over urine.

Examination of tissues removed at operation showed adenocarcinoma of prostate, of a portion of the seminal vesicle, and of lower portions of vasa deferentia. One excised gland was also carcinomatous. The trigone, the capsule of the prostate and perivesicular fat were free from disease.

III. A Clinical and Pathological Study of 40 Cases of Cancer of Prostate.

Nineteen of these are taken from the records of the Johns Hopkins Hospital, service of Dr. Halsted, whom I wish to thank for the privilege of reporting them. Twenty-one are from the records of my private cases.

Age.—The ages were as follows:

1				53 years.
8	between	55	and	59.
12	"	60	"	64.
11	"	65	"	69.
6	"	70	"	74.
1				75 years.
1				76 "

As seen here 57% are between 60 and 70 years of age and 95% between 55 and 75.

Onset.—In 28 cases the first symptom was frequency of urination; in 11 associated with more or less difficulty in voiding. Pain was noted at onset in only 12 cases and in four of these was only a slight burning in the bladder. Hematuria ocurred only three times at onset.

Later symptoms.—Pain was present in 27 cases, not present in 8, not noted in 5. It occurred 11 times in the bladder, 7 times in the penis, 4 times in the perineum and the rectum, three times each in the leg, thigh, sacrum, testicle, and abdomen, twice in the hip and groin and once each in the knee and sole of the foot. Cases in which a seminal vesicle was involved showed pain radiating at times down the sciatic nerve.

Hematuria.—This is stated to have been present in only 8 cases and in 4 of these the bladder was involved.

Retention of urine.—In all cases but one some residual urine was present. In 20 cases incomplete retention, varying from 50 to 850 cc. In 7 cases complete retention requiring catheter life and in 6 cases intermittent complete retention. In 8 cases no note was made on this point.

The prostate.—This was considerably enlarged in 24 cases, moderately enlarged in 9, slightly enlarged in 5, hard in 30, in places hard and in others soft in 5, and everywhere soft in 3 cases. It was nodular in 17 cases, smooth in most of the others. Marked tenderness was noticed only once in the 40 cases. In those cases which were not far advanced in the disease the prostate usually presented a smooth rounded surface, but was markedly indurated. This induration was often of stony hardness and the contrast with that of benign hypertrophy was very marked.

Seminal Vesicles.—It was in the region immediately above the prostate on each side in which the most significant changes were found, induration of one or both of the seminal vesicles being present in 29 cases. In recent cases, where more careful notes have been made, a plateau of induration in the intervesicular space has been noted in 10 cases. This induration is positive evidence of the spread of the disease between the vasa deferentia and the bladder after breaking through the capsule of the prostate at the base. Specimens show, however, that it is often well limited.

Rectum.—This was involved by the growth in but two cases and in only one of these was the mucous membrane ulcerated.

Bladder.—Careful cystoscopic examinations were made in 23 cases and in 7 the bladder wall was involved generally in the region of the trigone adjacent to one or both of the ureteral orifices, five times in the form of intravesical tumors, and twice of superficial ulceration. Examination of the bladder by suprapubic cystotomy showed a nodular elevation of the trigone in one case, the other case being normal. Two autopsies showed the bladder to be uninvolved. There was no intravesical enlargement of the prostate shown with the cystoscope in 5 cases. In 12 cases a very slight elevation of the median portion was present. In 3 cases a small median lobe, and in only one case a fairly large median lobe. The lateral lobes were at all intravesically enlarged in only four cases. In six cases the intravesical prostatic outgrowth was villous in type and associated with tumor of the bladder in 3 cases.

Glandular involvement.—Enlarged glands have been noted in only 11 of the 40 cases as follows: Deep pelvic glands four times, inguinal five times, iliac twice, sacral twice, axillary once, epitrochlear once. This corresponds to the findings of Kaufmann who discovered involvement of the pelvic glands in only 27 out of 100 autopsies. In one of our cases in which the tibiæ, vertebræ, and ribs contained numerous metastases, only one metastatic gland, and that a bronchial gland, was found.

Loss of weight was considerable in 18 cases.

Considerable increase in thickness of the suburethral portion of the prostate and also of the tissues between the trigone and the rectum has been shown in many of these cases by examination with the finger in the rectum and cystoscope in the urethra, the beak turned backward. In a number of cases the intervesicular mass and induration have prevented one from feeling the beak of the instrument in the bladder.

The pathology.—That carcinoma may begin in a benign adenomatous hypertrophy is shown in Case I. Generally induration is present in both lobes when the patient is first seen, but the disease remains localized within the prostatic capsule for months and often for several years. The capsule of the prostate is very thick and strong, especially in its posterior portion, where it is rendered much thicker and stronger by the incorporation of the aponeurosis of Denonvilliers, which covers intimately the posterior surface of the prostate and seminal vesicles. At the base of the prostate there is a space, between the seminal vesicles and the bladder, where the prostatic capsule is weakest and it is here in nearly all of the cases that the disease spreads first beyond the confines of the prostate. At the same time it usually travels up the lumina of the vasa deferentia and seminal vesicles forming a plateau of induration above the ordinary confines of the prostate, generally marked by a concave superior border and a notch on each side where it joins the lateral lobes. The posterior surface of the anterior part of the trigone becomes invaded from this mass, and it may finally penetrate the entire wall of the bladder and show itself intravesically generally as a small tumor or ulceration in the region of one or both ureteral orifices. The disease spreads laterally along the nerve sheaths and the lymphatics, indurated cords of which are often found leading upward and outward above the prostate along the lateral wall of the pelvis. The pelvic glands are, however, not often found involved.

Only occasionally does the disease present into the bladder

in the shape of considerable intravesical enlargements around the prostatic orifice.

IV. A Comparison with the Cases in the Literature in which Operations for Carcinoma were Performed.

I find 26 cases of primary carcinoma of the prostate reported, and to these six cases are here added, excluding those in which the Bottini operation was performed. Cases of carcinoma of the rectum involving the prostate and sarcoma of the prostate, which have been included by Oraison, Pousson, and Hawley, have no place here, but I have referred to them briefly to show why they should be excluded. I have grouped the cases according to the operation performed as follows:

Partial operations, (enucleation, partial excision or curettage), by perineal route, 12 cases, by the suprapubic route 9 cases.

Radical operations.—A. Complete excision of the prostate, the entire bladder and the seminal vesicles with transplantation of the ureters into the rectum, one case, by Küster, with death in 5 days.

B. Complete excision of the prostate, probably the seminal vesicles, most of the bladder with transplantation of the ureters into the remaining vertex of the bladder, one case, Harris. Recurrence and death two months later of pneumonia.

C. Complete excision of prostate, seminal vesicles, adjacent portion of the bladder leaving the ureters intact and anastomosing bladder opening to membranous urethra, four cases, Young (reported above).

D. Excision of prostate without seminal vesicles, three cases. Immediate death, one case. Recurrence and death in the other two cases.

E. Rectum and prostate involved by carcinoma, 5 cases. Immediate death, 3 cases. Two cases of primary carcinoma of the rectum involving only slightly the prostate, said to be cured after operation.

F. Sarcoma of the prostate, three cases. Immediate death, one case. Recurrence and death 9 months and four years, two cases.

Remarks.—A study of these cases shows conclusively that partial operations are of no permanent utility in cancer of the prostate. Among the 12 cases in which partial operation was done through the perineum, 9 died of recurrence and the other three cases were followed only one, three and nine months respectively. Of the 9 operated upon by the suprapubic route 6 had recurrence, one was not followed and two were said to have been fully cured one year after the operation, although only a median lobe was removed in each case. In the three cases in which the prostate was completely excised, but the seminal vesicles and the adjacent portion of the trigone were not removed, death resulted in all three cases, once from operation, twice from recurrence.

Küster's case associated with multiple vesical tumors cannot rightly be included in the results of operations upon the cancerous prostate. His operation of complete excision of the bladder and prostate, with transplantation of the ureters into the rectum ended in death in 5 days. When the disease has spread beyond a localized invasion of the bladder adjacent to the prostate, a radical operation is out of the question, and such procedures as that of Küster are useless if not always certainly fatal. Those in which the rectum is invaded in the prostatic tumor are in the same category—useless and harmful. Of the five cases reported only one was cured and in this case the carcinoma started in the rectum and involved the prostate only superficially. Harris' case is very interesting, but simply shows the truth of the above statements. The remaining class—those in which the seminal vesicles and cuff of the bladder were excised in one piece with the prostate, comprises only the four cases of the writer. There has been no operative mortality. One case (VIII) died six weeks after the operation as a result of an operative mistake—excision of the lower half of the intramural course of the ureters along with the trigone because it felt like it was invaded. Careful study of the specimen removed, however, showed that this was a mistake; that the trigone was only invaded near the prostatic orifice, and that the excision had been much more extensive than was necessary. This was fully confirmed at autopsy as careful search failed to reveal any carcinoma, regional or glandular, and sections of structures adjacent to the prostate were negative microscopically. This case would probably have been cured by the operation had the valvular ends of the ureters not been removed.

Case VII died one year later as a result of litholapaxy. The operative specimen in this case showed cancer up to the upper limit of excision (above the left seminal vesicle) and the autopsy showed a very small area of carcinoma behind the bladder above this point. No invaded glands and no other evidence of cancer was to be found. The case had been subjected to a Bottini operation, in another city, three months before. A radical operation at that time would probably have cured him.

The other two cases (IX, X) have been operated upon 6 and 2 months respectively—too recent for consideration; however, both are comfortable and free from recurrence so far. It has been surprising to see how easily this deep and extensive operation can be carried out and particularly how little post-operative shock and discomfort is caused.

Early diagnosis.—The question of cure depends upon early diagnosis. As shown above, this is often difficult because of the absence of characteristic symptoms and signs. When severe pain and hematuria are associated with a very hard prostate with upward prolongation of the induration into the region of the seminal vesicles on each side the nature of the disease is evident at once. When, however, the symptoms are those of ordinary hypertrophy and the seminal vesicles and the vesicular region are normal in feel the diagnosis is often difficult. After a careful review of these cases I now feel that a markedly indurated prostate producing obstruction in a man over 50 years of age should be viewed with suspicion. If it is of stony hardness it is very apt to be cancerous, especially if the cystoscope shows little or no enlargement intravesically as in the ordinary hypertrophy. In

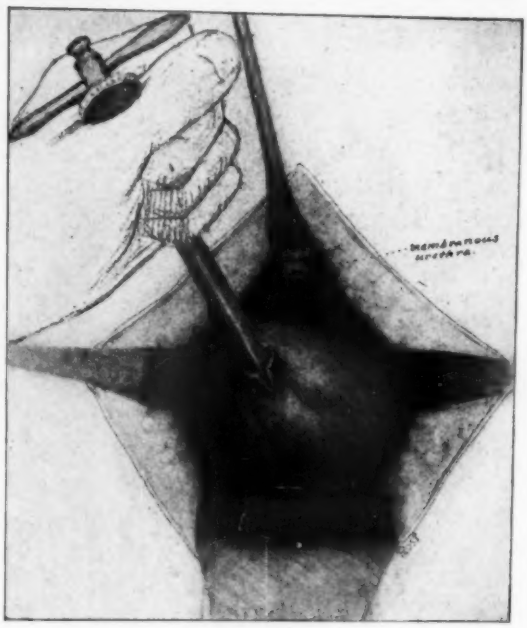

FIG. 1.

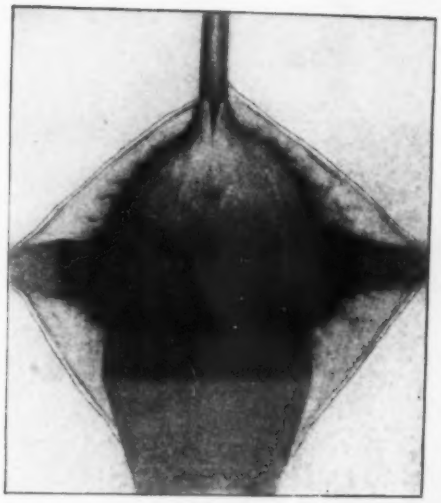

FIG. 2.

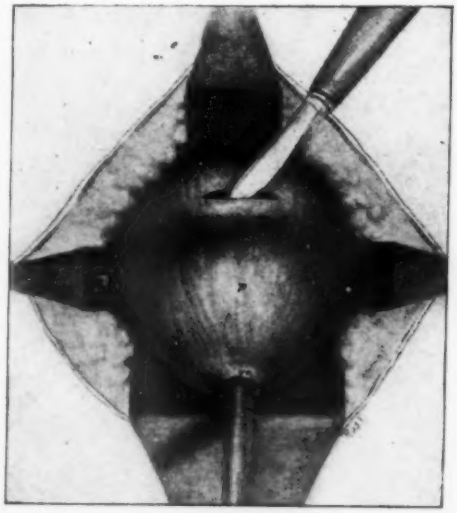

FIG. 3.

FIG. 4.

FIG. 5.

FIG. 6.

FIG. 7.

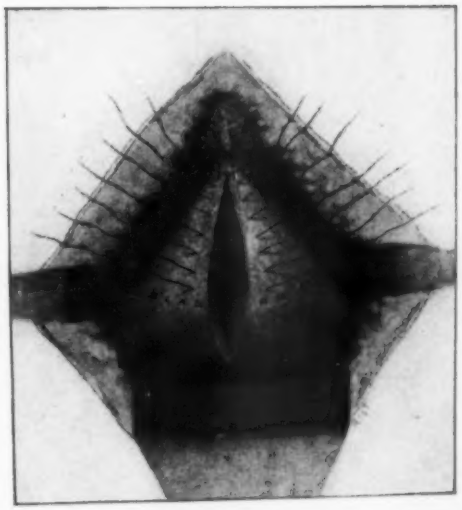

FIG. 8.

such cases I proceed to expose the posterior surface of the prostate as in the ordinary prostatectomy operations, palpate the prostate directly and if I find the posterior capsule more adherent to the rectum, the tissues more hemorrhagic and the consistency of the prostate much more indurated than in simple hypertrophy, I am able generally to make the diagnosis of carcinoma without cutting into it, and proceed at once with the radical operation.

In a recent case after exposing the prostate I was still uncertain as to malignancy and therefore made a longitudinal incision into the prostate on each side of the urethra as if for the usual prostatic enucleation, and then excised a slice of the lateral lobe parallel to the cut. Macroscopic examination of this showed the characteristic appearance of prostatic carcinoma—glandular yellowish dots and lines in a paler, more fibrous stroma, and a frozen section, made at once and stained, showed definite adenocarcinoma invading the intra-glandular stroma. It only required 6 minutes to make and stain the frozen section, and I therefore propose the method as one of practical utility in all cases where the operator is in doubt as to the character of the enlargement. When the presence of cancer is demonstrated the capsular incisions are to be closed at once and the radical operation carried out.

In view of the six cases detailed at the beginning of this paper in which a mistaken diagnosis was made I propose in all cases in the future to study the cut surface of the prostatic lobes immediately after their enucleation at the operating table, and if there is the slightest suspicion of malignancy to have frozen sections made at once. In very few cases will the wait of 5 minutes or more make any difference to the patient. In cases where the prostate is indurated, if only in part, this operating-room-study of the fresh tissues is of the greatest importance. I feel sure that several of my first six cases might have been saved by the radical excision which would now follow such a course.

Conclusions.

The following conclusions may be drawn from this study of 40 cases. Carcinoma of the prostate is more frequent than is usually supposed—occurring in about 10% of the cases of prostatic enlargement, as shown also by Albarran. It may begin as an isolated nodule in an otherwise benign hypertrophy or a prostatic enlargement which has for many years furnished the symptoms, and signs of benign hypertrophy may suddenly become evidently malignant.

Marked induration, if only an intralobar nodule in one or both lobes of the prostate in men past 50 years of age should be viewed with suspicion, especially if the cystoscope shows little intravesicular prostatic outgrowth, and pain and tenderness are present.

The posterior surface of the prostate should be exposed as for an ordinary prostatectomy, and if the operator is unable to make a positive diagnosis of malignancy, longitudinal incisions should be made on each side of the urethra (as in prostatectomy) and a piece of tissue excised for frozen sections, which can be prepared in about six minutes and examined by the operator at once. If the disease is malignant the incisions may be cauterized and closed and the radical operation performed.

Cancer of the prostate remains for a long time within the confines of the lobes, the urethra, bladder and especially the posterior capsule of the prostate resting inviolate for a considerable period. Extraprostatic invasion nearly always occurs first along the ejaculatory ducts into the space immediately above the prostate between the seminal vesicles and the bladder and beneath the fascia of Denonvilliers. Thence the disease gradually invades the inferior surface of the trigone and the lymphatics leading toward the lateral walls of the pelvis, but involvement of the pelvic glands occurs late and often the disease metastasises into the osseous system without first invading the glands.

Cure can be expected only by radical measures and the routine removal of the seminal vesicles, vasa deferentia and most of the vesical trigone with the entire prostate as carried out in four cases by the writer and fully described by the illustrations is shown to be necessary by the 40 cases, including 8 autopsies and 10 operations, reported above.

The four cases in which the radical operation was done demonstrated its simplicity, effectiveness and the remarkably satisfactory functional results furnished.

ACTION OF THE TOXIC AGENT OF LOBAR PNEUMONIA: THERAPEUTICS.[1]

By Walter V. Brem, Jr., M. D.,

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Introduction.

The data that have been accumulated during this study are incomplete and, consequently, the inductions made therefrom are often inconclusive. Nevertheless, since many definite questions for further investigation have arisen, it has seemed worth while to present the facts, together with their possible interpretations and therapeutic indications.

In discussing the changes in functional activity occurring in pneumonia, it has been found convenient to divide the cases here presented into two groups, according to the gravity of the symptoms. To the first group belong the mild cases;

[1] Read before the Johns Hopkins Medical Society, June 5, 1905.

to the second, the severe and fatal cases. For convenience, also, the causative factor, which in this disease brings about the changes in question, will be designated as the toxic agent. The dots in the curves of the charts here studied represent, for the most part, averages of daily two-hour observations. But dots in blood-pressure curves and in every place where the hour is stated represent only single observations. The blood-pressure instrument used was the Riva-Rocci with 12 cm. cuff. Normal systolic and diastolic blood-pressures are those determined by Brush (1). Systolic pressure was obhours preceding improvement, at which time all the other curves fall synchronously. Besides these phenomena, there are nervous manifestations at onset or during the acute illness, namely, headache, chill, restlessness, wakefulness, convulsions frequently in children, and occasionally active delirium; all manifestations of excitation of the central nervous system.

Respiration.—Acceleration of the respiratory-rate may be due to one or more of several causes, chief of which are pain, fever, and toxæmia (Osler). Pain in the side, exaggerated

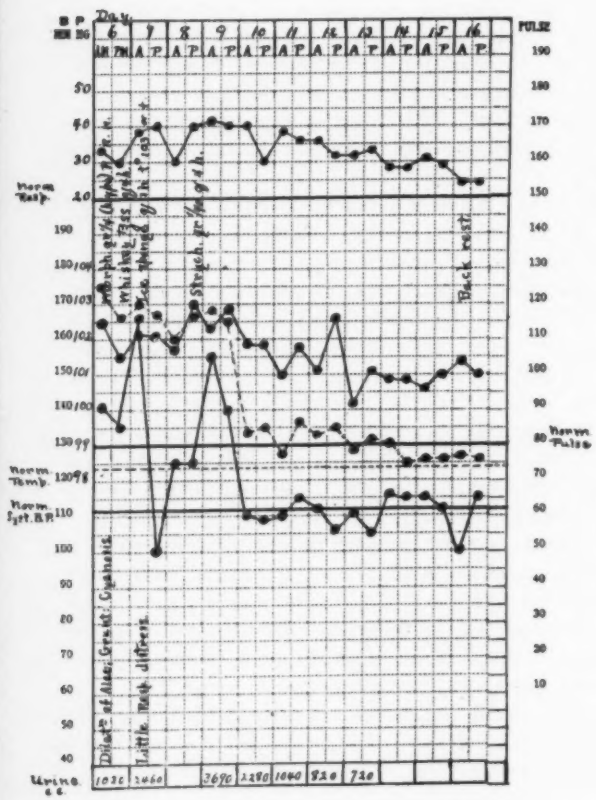

CHART I.—Merriweather, male, colored, age 56, recovery.

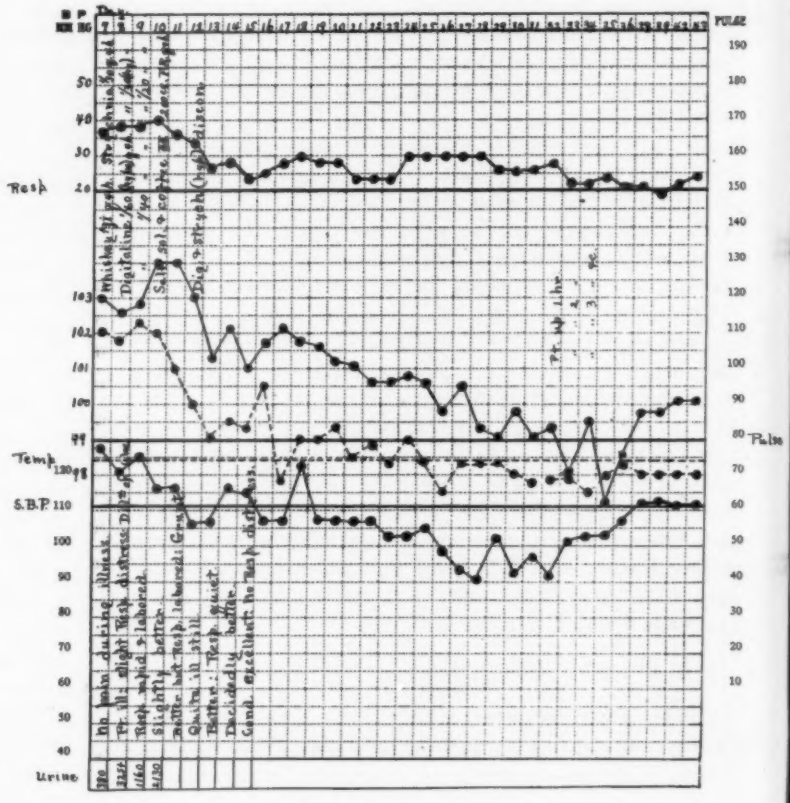

CHART II.—Jenkins, male, colored, age 28, recovery.

served by the method of obliteration; diastolic, by Strassburger's method (2). All cases studied, except one (Chart V), were under my immediate care in the wards of the Johns Hopkins Hospital.

MILD ACTION OF THE TOXIC AGENT.

The mild cases are represented by Charts I, II, V, VII, which show a series of familiar phenomena. Here, the temperature is elevated; the respiratory-rate and pulse-rate are accelerated; and both systolic and diastolic (Chart VII) blood-pressures are high. The urinary output is diminished at first, but there is a great increase during the twenty-four

by breathing, causes voluntary restriction of the respiratory movements and there is compensatory hastening. But cases having no pain (Charts II, VII), and others in which pain has been relieved by the ice bag and analgesics, show similar acceleration. Fever, also, aids in producing the condition; but not infrequently it happens that the respiratory-rate increases while temperature falls or remains unchanged, or the change in one is not in proportion to the change in the other (Charts III, IV, X). Moreover, in typhoid fever, when temperature reaches a high degree, there is no similarly marked acceleration of the respiratory-rate, which often remains normal throughout the course of the disease. It is easier to

think, therefore, that the respiratory-rate is not greatly dependent upon either pain or temperature, but that the acceleration is in response chiefly to the action of the toxic agent upon the respiratory center.

In addition to acceleration of the rate, one finds by examination of the patient that the accessory respiratory muscles are brought into action, there is an expiratory grunt and dilatation of the alæ nasi with inspiration, and the vesicular murmurs in uninvolved portions of the lungs are intensified. It appears, then, that there is an increase not only in the rate but in the intensity, also, of the respiratory movements; that is, there is hastened and intensified activity of the respiratory center. Therefore, the action of the toxic agent upon the center may be regarded as that of a stimulant.[3]

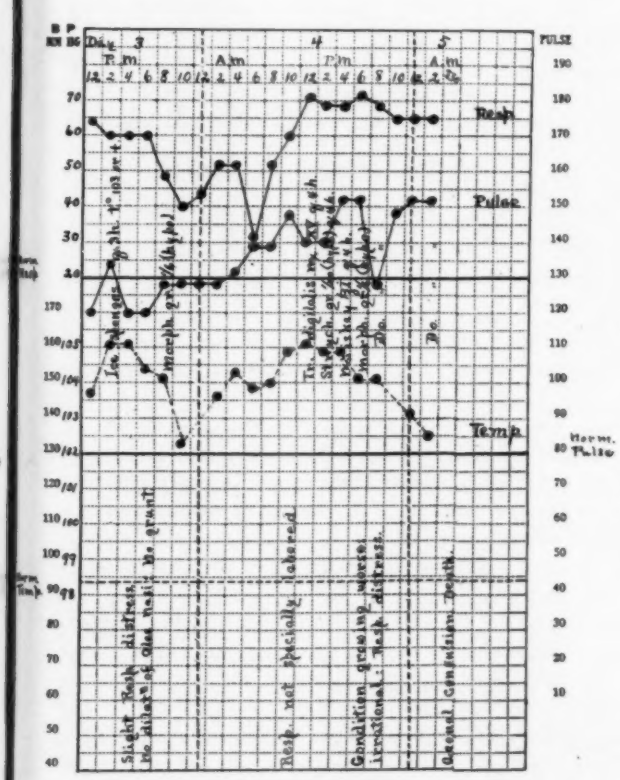

CHART III.—Bunch, male, colored, age 23, death.

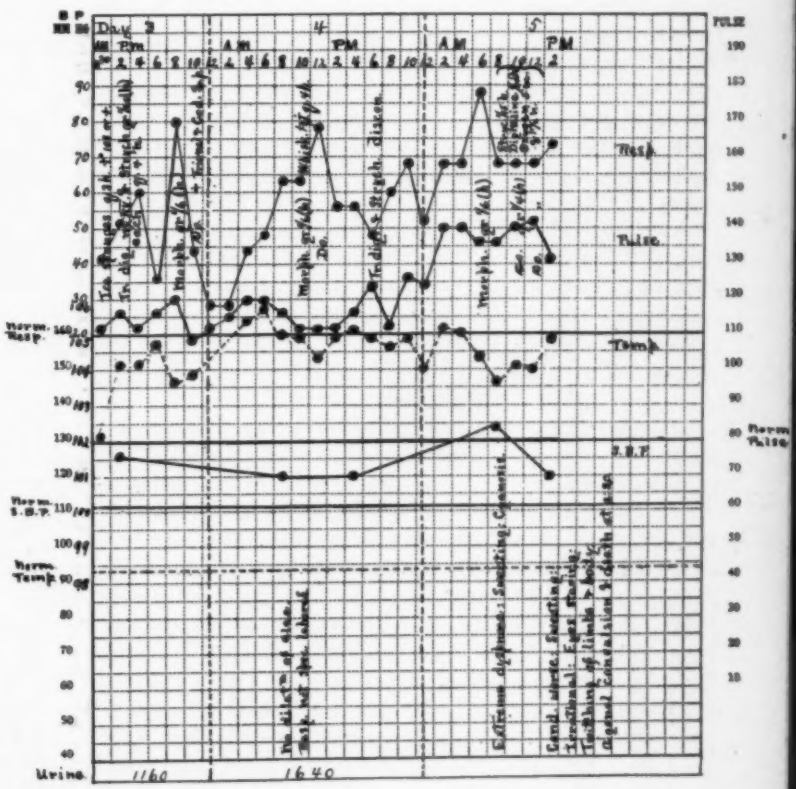

CHART IV.—Harris, male, colored, age 38, alcoholic, death.

Circulation.—The circulatory phenomena are acceleration of pulse-rate and high systolic blood-pressure. Diastolic blood-pressure, likewise, in the one case in which observations were made, was high, but this cannot be used as a demonstration that it is usually elevated. Evidence of high pressure in the pulmonary vessels, also, may be found in the almost constant accentuation of the pulmonic second sound.

Acceleration of pulse-rate may result partially from pain, restlessness, and fever. The rate remains rapid, however, when pain and restlessness are absent (Charts II, VII) or relieved (Charts I, III, IV, IX, X). These charts show further that, like the respiratory-rate, the pulse-rate does not vary constantly with temperature, but that very wide differences frequently occur. Therefore, it is probable that this disturbance, also, is due chiefly to the action of the toxic agent upon the circulatory mechanism. It may result from depression of the cardio-inhibitory center or from increased irritability of the heart muscle, of the cardio-accelerator center, or of both.

Depression of the cardio-inhibitory center would offer a sharp contrast to the general nervous excitation and apparent stimulation of the respiratory center, while in perfect harmony with other phenomena is the supposition that the action of the cardio-inhibitory center, even if its irritability be increased, is overborne by the more intense action of the toxic agent upon the heart muscle and accelerator center. Some

[3] "Drugs which increase the activity of any organ or function are said to *stimulate* it. Stimulation is properly used to indicate an increase in the specialized function of a cell. . . . Irritation, on the other hand, is used rather in reference to the changes in the conditions common to all forms of living matter, that is, it indicates a change in the growth and nutrition of the cell, rather than in the specialized functions" (Cushny). The terms will be used in these senses throughout the present paper.

confirmation, possibly, of this view may be found in the fact that digitalis, exhibited during the stage of excitation, does not slow the pulse-rate. This seems to indicate that there are forces present which counteract the primary stimulating action of the drug upon the cardio-inhibitory center.

Besides rapidity of heart-rate, examination of the patient reveals a strong cardiac impulse and loud heart sounds with marked accentuation of the pulmonic second. The group of phenomena strongly suggest intensified cardiac activity and increased work. This is rendered the more probable by the fact that systolic blood-pressure is high; for an increase of systolic pressure indicates an increase of cardiac work, unless there is a greater rise of diastolic pressure. That the rise of diastolic pressure during this stage of pneumonia is not as great as that of systolic pressure is indicated by the large, bounding pulse. Such a pulse, with systolic pressure high, means a large cardiac output and an increased product of the formula for cardiac work (mean blood-pressure by cardiac output).

Summary.—The mild action of the toxic agent possesses, then, all the features of a stimulation of the central nervous system and heart muscle, evidence of which is found in cerebral excitation and in increased activity of the respiratory and circulatory mechanisms.

Intense Action of the Toxic Agent.

In the severe and fatal cases (Charts III, IV, IX, X) the phenomena vary in different individuals according to the relative susceptibility of different organs. Often there is evidence of cerebral depression, which results, if the theory of stimulation be correct, from overstimulation and enfeeblement. The patient looks toxic, there are stupor, low delirium, later coma, and occasionally involuntary passage of urine and fæces. In other cases the mind may remain active until the end. Temperature may rise before death (Chart IV, day 5, 2 p. m.), or suffer a decided fall (Chart III, days 4 and 5); again it may remain practically unaffected while the respiratory or circulatory condition is grave (Charts IX, days 4, 5, 6, 7; X, days 8, 9). These variations, also, may depend upon the degree of excitation and overstimulation of the heat-regulatory centers.

Respiration.—It is probable that in the majority of cases the respiratory function is that most gravely affected. The rate usually ranges between 40 and 80 per minute; the accessory muscles of respiration are brought more violently into action; the vesicular murmurs become more intense; the movements become progressively shallow; breathing necessitates great effort and becomes labored; and cyanosis appears, evidence of deficiency of O and accumulation of CO_2 in the blood, a condition which may be termed respiratory insufficiency.

It is an interesting and important point that respiratory insufficiency may become established even under strong stimulation when the total quantity of air respired is much increased. The factors concerned in this are two: (1) The depth of the respiratory movements tends to vary inversely with the rate, and (2) the capacity of the bronchial tree, about 140 cc., remains a constant figure, while the tidal wave of respiration decreases in volume; that is, the quantity of fresh air actually entering the alveoli with inspiration is the portion of respired air that suffers diminution when the volume of the tidal wave is decreased.[3] Bearing these facts in mind, a glance at the table below will show that, with progressively rapid and shallow movements, the alveolar portion of respired air diminishes with far greater rapidity than the total volume of the tidal wave.

TABLE I.

Condition	Tidal wave × Rate per min. = Total per min.	Capacity of Bron. tree	Alveolar portion of tidal wave × Rate per min. = Total per min.	%	Equivalent volume % of atmospheric O
1. Normal	500 × 20 = 10,000cc.	140cc.	360 × 20 = 7200cc.	100	21.0
2. Depth in exact inverse proportion to rate	250 × 40 = 10,000cc.	140cc.	110 × 40 = 4400cc.	61+	12.8
3. Stimulation	200 × 60 = 12,000cc.	140cc.	60 × 60 = 3600cc.	50	10.5
4. Strong stimulation	190 × 80 = 15,200cc.	140cc.	50 × 80 = 4000cc.	55.5	11.6+

Now, 13 volume per cent of atmospheric O is necessary to raise alveolar O-tension to the point where normal O-absorption by blood occurs. In conditions 3 and 4, the alveolar O-tension is reduced to 50 and 55.5 per cent, respectively, of normal; that is, to points equal to alveolar O-tension that would be produced by atmospheres containing only 10.5 and 11.6 + volume per cent of O. Therefore, in conditions 3 and 4, there is respiratory insufficiency, although the total volume of air respired is increased considerably in the former condition and greatly in the latter. The table deals only with mechanical mixture of the gases, which is of far greatest importance in the interchange between the atmospheric and alveoli (4). As to the less important factor of diffusion, it can be shown by another calculation that, if the inspired air enters the alveoli gradually and with but slight mechanical mixture, diffuse conditions are correspondingly less efficient with rapid and shallow respiratory movements.[4] Owing to the same causes there is diminished elimination of CO_2 with corresponding increase of alveolar CO_2-tension, and consequent accumulation of this gas in the blood. There is added, thus, to the action of the toxic agent an intensification of the

[3] It is true that a volume of air equivalent to the tidal wave, normally about 500 cc., does enter the alveoli with each inspiration. But the first portion entering is the 140 cc. of vitiated alveolar air that filled the bronchial tree at the end of the preceding expiration. Therefore, in a normal inspiration, only 360 cc. of atmospheric air enters the alveolar. So, in any given inspiration, the alveolar portion of respired atmospheric air may be obtained by subtracting 140 cc. from the volume of the tidal wave.

[4] Rapidity of diffusion varies with the area and with the time of contact. Since a smaller quantity of air enters the alveoli with rapid and shallow breathing, the time of its passage in and out is correspondingly less. The area of contact cannot be estimated, but it is probable that it, also, is reduced somewhat.

natural physiological stimulus to the respiratory center. This tends further to increase its work and to lessen the efficiency of respiration. A vicious circle is thereby produced and enfeeblement of the center follows, passing on rapidly towards asphyxiation or exhaustion.

Circulation.—The circulatory condition may, and often does, remain excellent throughout, and, as a rule, the circulatory mechanism is much less affected than the respiratory. The pulse-rate, under more intense action of the toxic agent, becomes more markedly accelerated (Charts III, days 4, 5; IV, days 4, 5; IX, days 6, 7; X, days 7, 8, 9). But even with great acceleration, systolic blood-pressure may remain above normal until the end (Chart IV, days 3, 4, 5), indicating that the heart's action has not become enfeebled.

In other cases, the circulatory mechanism may bear the brunt of the attack or be affected simultaneously with the respiratory mechanism. In addition to the rapid pulse-rate, systolic blood-pressure falls even if there be associated respiratory insufficiency with asphyxial stimulation of the vaso-constrictor center (Chart IX, days 4, 5, 6); the extremities become cyanosed; the pulse becomes "thready," indicating lessening of pulse-pressure with which the urinary output tends to vary (3); the heart's action becomes enfeebled and the sounds soft, the pulmonic second loses its accentuation, and the right ventricle may become dilated. These phenomena are to be accounted for, apparently, by overstimulation and overwork leading to enfeeblement and insufficiency of the circulatory mechanism. The probable results are lessened metabolism and lessened power of resistance; decreased urinary output with decreased elimination of the toxic agent; and sometimes the onset of œdema of the lungs, which may be the terminal event. In other cases, enfeeblement of the mechanism may pass on quickly to exhaustion and death.

Systolic blood-pressure, it has been said, falls with the establishment of circulatory insufficiency, even if there be an associated condition of respiratory insufficiency (Chart IX, days 4, 5, 6). If, however, the circulatory condition remains good when respiratory insufficiency becomes established, systolic blood-pressure rises, owing to asphyxial stimulation of the vaso-constrictor center (Charts IV, day 5; IX, day 7; X, day 9). The change in blood-pressure of Chart IX, day 7, was due to the administration of digitalis every four hours. It appears that the drug improved the condition of the heart so that blood-pressure became elevated, as is normally the case with asphyxial stimulation. It is evident, therefore, that systolic pressure may be either high or low when the situation is critical, and that in itself it is of little value as an indicator of the patient's condition. Considered with the respiratory phenomena, however, it is of great value in determining the circulatory condition and the treatment to be pursued.

Summary.—The phenomena of the mild action of the toxic agent pass over into phenomena of the more intense action. These appear to be expressions of intensified stimulation, which aggravates the condition of increased functional activity and tends to induce overwork, enfeeblement and exhaustion. The mechanisms concerned break down prematurely because they have been subject, also, to the irritative destructive action of the toxic agent.

The main causes of death are (1) respiratory insufficiency terminating in asphyxiation or in exhaustion of the respiratory center, and (2) circulatory insufficiency, which leads, presumably, to accumulation of the toxic agent, and which may induce œdema of the lungs or end in exhaustion of the heart muscle.

Therapeutics.

Having studied in typical cases the changes in functional activity brought about by the action of the toxic agent, one is now in a position to discuss measures to be used in combating its influence. The ideal therapy, of course, would be to prevent destruction of tissues by neutralizing or destroying the toxic agent, but with the possibility of this the present study is not concerned. In lieu of it, efforts must be directed towards eliminating the agent or ameliorating its harmful influences.

Elimination.—Undoubtedly the most efficient means of eliminating the toxic agent is by *internal hydrotherapy*. The effort is made to pass through the circulation the largest quantity of fluid possible in the hope that as it is passed through the kidneys the toxic agent will be carried, in one way or another, along with it. If there is a soluble toxin, this is a reasonable hope; for during the acute illness, almost constantly the albumin molecule, a normal constituent of blood, passes through the kidneys. Since an effort is made to eliminate abnormal substances in blood, it is reasonable to suppose that the abnormal toxin molecule would be more readily eliminated than the normal albumin molecule. If there is no soluble toxin, *B. typhosus* sometimes, at least, passes through the kidneys, why not *Pneumococcus?* In reference to this point, it is possible that failure to grow *Pneumococcus* from urine has been due to the fact that the organism dies out quickly in an acid medium. Should the urine be rendered alkaline, possibly results would be different.

In the mild cases studied, it was shown that during the twenty-four hours preceding improvement there was an increase in the urinary output. Chart V illustrates this to a marked degree. The case was a particularly favorable one for a test. The patient was an orderly in the hospital and was admitted on the first day of his illness. He had been famous for his earnestness in administering water to typhoid fever patients, and was responsible for the phenomenal urinary record of 25,400 cc. in twenty-four hours. When he, himself, was told to drink freely, he did so. Whether or not this was the causative factor, the fact remains that between the third and fourth days of his illness, his temperature dropped from 104.3° to 100.5°, his respiratory-rate from 35 to 24 per minute, his pulse-rate from 124 to 100, and his systolic blood-pressure from 135 mm. Hg. to normal.

It is conceivable that a large proportion of the toxic agent was thus eliminated, and that the toxic agent which remained produced phenomena similar to those which would be pro-

duced by a small dose. The temperature, respiratory and pulse curves of the chart do not return to normal until the tenth day, when, it is probable, elimination was complete or an immunity had become established. Chart I presents phenomena almost exactly similar to these; Charts II and VII, to a less degree. It is regrettable that none of the figures of the urinary output can be relied upon absolutely, but they are strongly suggestive, nevertheless, that *internal hydrotherapy* may be of the very greatest value.

Another measure, to be discussed later, which may aid

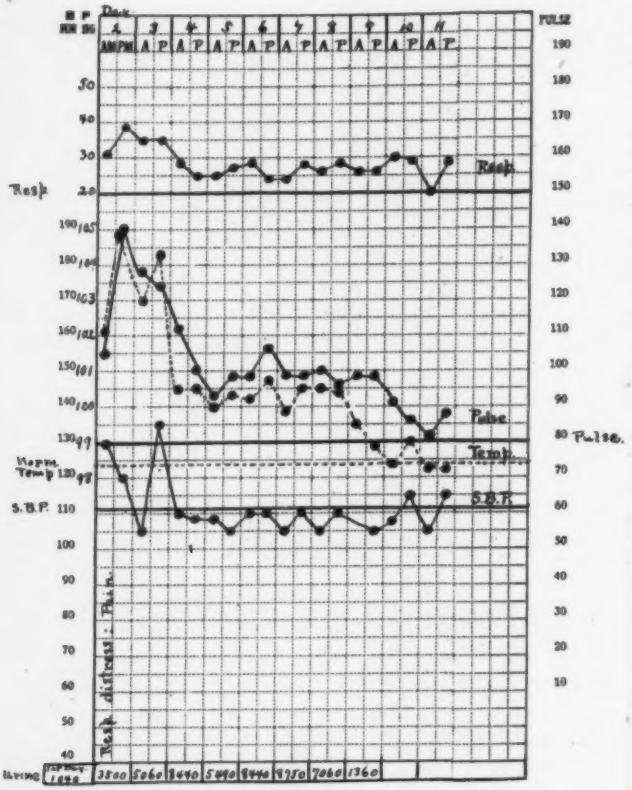

CHART V.—Linzey, male, white, age 32, heart lesion, recovery.

materially in elimination, is the administration of *digitalis*. This drug increases the urinary output through its beneficial influence upon the circulatory condition.

Amelioration of harmful influences.—Next to elimination, it is desirable to combat disturbances induced by the action of the toxic agent. Fever is met best by *external hydrotherapy;* pain may be relieved by the *ice bag* and *analgesics;* restlessness, insomnia, and delirium, by *external hydrotherapy, analgesics,* and *narcotics.* Special attention is demanded by the respiratory and circulatory conditions.

Respiration.—In accordance with the conclusions reached regarding the respiratory disturbances, it is evident that the indication is to counteract the stimulation of the respiratory center. But, if the respiratory-rate were decreased and shallow movements persisted, only a more deplorable condition would ensue. The depth of the respiration must be increased, if possible, as well as the rate slowed.

(*a*) *Heroin.*—In animal experimentation, it has been found that *heroin* in small doses reduces the respiratory-rate 30 to 50 per cent, while the depth of each movement is so greatly increased that the total volume of air respired in a unit of time is greater than before its administration. In man, *heroin* has been used to a certain extent for this action,

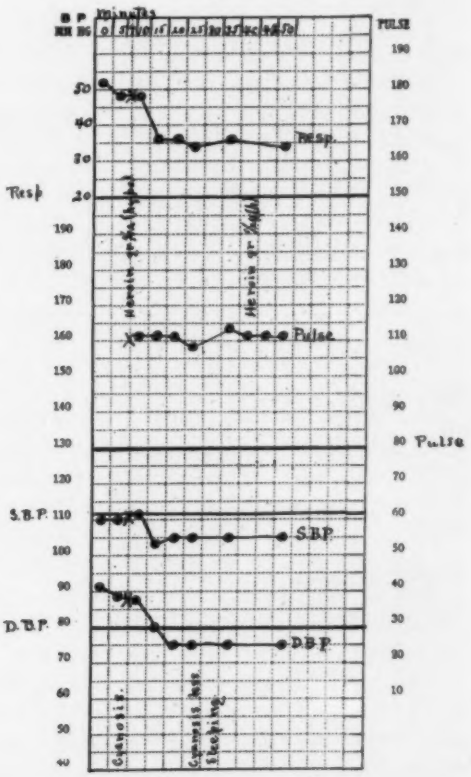

CHART VI.—Fazio, male, white, age 28.

though not nearly as much so as for its influence upon cough. If the results observed in animals could be obtained in pneumonia cases and that without untoward effects, it seemed that in this drug would be found an almost perfect physiological antidote to the toxic agent; for not only would it meet the demands of the respiratory condition, but, also it would relieve pain and cough, allay restlessness, and produce sleep.

Heroin hydrochlorate, gr. $\frac{1}{12}$, was administered hypodermically to a patient having rapid, somewhat shallow respirations (Chart VI). In eight minutes, phenomena typical of *heroin* were induced; the depth of the respiratory movements increased as the rate fell, cyanosis cleared somewhat, blood-pressure became lower, and the patient slept. One-half an

hour later, gr. $\frac{1}{14}$ was given hypodermically, and after another hour, gr. $\frac{1}{12}$, making in all gr. $\frac{1}{6}$. Following this, two more doses of gr. $\frac{1}{4}$, each, were administered hypodermically at intervals of four hours. No untoward symptoms supervened in spite of the rather large doses, and it was thought that a tolerance for the drug might be exhibited by pneumonia patients.

To the next patient, the *hydrochloride* was administered hypodermically on three successive days. The first day, gr. $\frac{1}{14}$ was given three times at half hour intervals, the results being

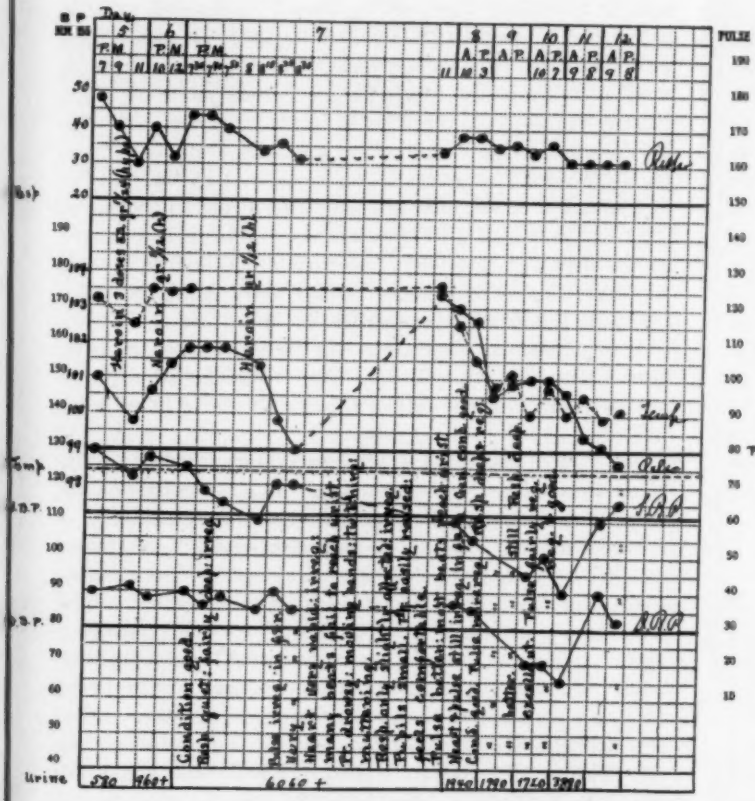

CHART VII.—Hughes, male, white, age 44, alcoholic, recovery.

similar to those seen in the first case, though not so marked. There were no untoward effects. The second day, gr. $\frac{1}{12}$ was given in a single dose, and still there were no bad results. The third day (Chart VII, day 7), gr. $\frac{1}{12}$, again, was given. There was no respiratory insufficiency at the time. The rate became slower as before and the depth of the movements increased. But, within twenty minutes the pulse began to drop a beat occasionally, then intermissions became more frequent, and the pulse became irregular in force and rhythm. In thirty minutes after the administration, only 80 beats per minute reached the wrist, while by auscultation 132 cardiac contractions per minute were counted. The heart's action, also, was alarmingly irregular in force and rhythm, having the characteristics of so-called delirium. The respiratory condition and general condition of the patient remained good and he slept quietly, being unaware that anything was wrong. The heart improved gradually during three days until its action became regular and the heart-rate and pulse-rate equal. Recovery was good.

The condition could scarcely have been induced by depression of the cardio-inhibitory center, for section of the vagi does not affect the regularity of the cardiac rhythm, the vagus influence affecting only rate; nor was any apparent benefit

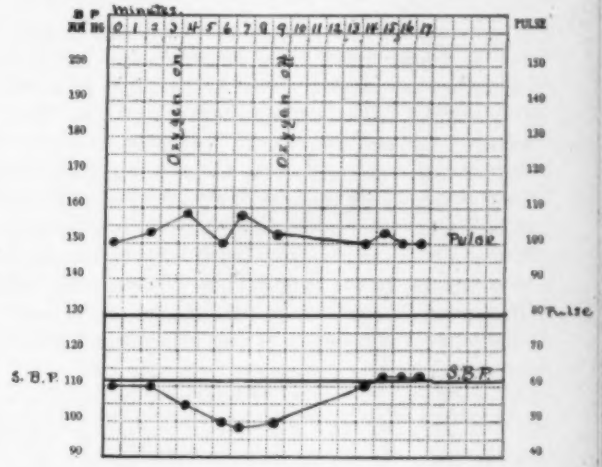

CHART VIII.

derived by stimulation of the center with *digitalis*. It is probable that the untoward effect resulted from some obscure action of the drug upon the heart muscle.

In the literature that has been examined, every report in which the action of *heroin* on the cardio-vascular system is discussed states definitely that the drug has no depressing action, some observers holding that it has a favorable influence comparable to that of *morphine*. One observer finds it the best remedy that he has used in the treatment of pneumonia (5). Another reports that he has used it hypodermically in three hundred unselected cases, doses ranging between gr. $\frac{1}{12}$ and gr. $\frac{1}{4}$, and that only in the larger doses have untoward symptoms developed. These consisted of

nausea, vomiting, malaise, lassitude, and sleep (6). No mention is made of circulatory disturbances.

Considering the phenomena of the action of the toxic agent of the disease, it is difficult to believe that pneumonia renders a patient more susceptible to the action of *heroin*. Against the view are the results obtained by previous administrations, the report cited above, and the fact that in the great majority of cases the disease establishes a decided tolerance for *heroin's* parent drug, *morphine*. The patient in question had a moderate alcoholic history, and it may be that this was a predisposing factor. A third possibility seems most plausible, although one dislikes to use it, that is, the case was one of individual idiosyncrasy. At any rate, the case is sufficient to demand great care in the exhibition of the drug in pneumonia, especially in alcoholic patients. If, however, it can be shown that the disease causes no special susceptibility to the action of *heroin*, the drug should be a remedy of great value in meeting both the respiratory and general indications.

(*b*) *Morphine.*—Instead of *heroin*, should its contraindication be demonstrated, there remains *morphine*, the equal of *heroin* in every respect, except in its action upon the respiratory center. Like the former drug, *morphine* slows the respiratory-rate and deepens the movements, though it does not increase the depth sufficiently to prevent a diminution of the total volume of air respired in a given time (Cushny). But, if individual respirations are deepened sufficiently, the total volume of air entering the alveoli may be increased in spite of a decrease in the total volume respired. The table below illustrating this point is just the reverse of the previous table illustrating the progress of respiratory insufficiency.

TABLE II.

Condition	Tidal wave × Rate per min. = Total per min.	Capacity of Bron. tree	Alveolar portion of tidal wave × Rate per min. = Total per min.	%	Equivalent volume % of atmospheric *O*
1. Toxic stimulation	200 × 60 = 12,000cc.	140cc.	60 × 60 = 3600cc.	50	10.5
2. Action of morphine ..	250 × 40 = 10,000cc.	140cc.	110 × 40 = 4400cc.	61	12.8
3. Strong action of morphine.....	300 × 30 = 9,000cc.	140cc.	160 × 30 = 4800cc.	66.6	14

Condition 1 supposes respiratory insufficiency brought about through stimulation of the respiratory center by the toxic agent. In condition 2, under the action of *morphine*, the total volume of air respired in one minute is decreased 2000 cc., but the total volume entering the alveoli is increased 800 cc., bringing alveolar *O*-tension to a point equal to the tension that would be caused by an atmosphere containing 12.8 volume per cent of *O*, and respired under normal conditions. This is on the border between sufficiency and insufficiency; for, it has been said, an atmosphere containing 13 volume per cent of *O* is required, under normal conditions of respiration, to raise alveolar *O*-tension to the point of normal *O*-absorption by blood. In condition 3, the total volume is decreased 300 cc., but sufficiency is completely restored by the greater volume reaching the alveoli. Though these figures are purely hypothetical, they suggest that *morphine*, also, may be of great value in meeting respiratory indications. Moreover, as stated above, experience has shown that in pneumonia it is well borne in the majority of cases, and that, as a rule, large doses may be given without untoward effects. Like *heroin* it relieves, also, the pain, cough, and restlessness.

By consulting the charts, it may be seen that in the mild cases the respiratory-rate rarely rose above 40 per minute, while in the severe and fatal cases it ranged between 40 and 80. A rate of 40, then, appears to be upon the line of danger, and, as a working basis, efforts should be directed towards preventing an acceleration up to this point. I should suggest, therefore, the administration of *heroin* or *morphine* in small doses every two hours for a respiratory-rate of 36 or greater, the dose to be gradually increased in size until the physiological action is obtained or untoward symptoms supervene. It should be remembered, however, that the rapidity of respiration is not, after all, the factor of most importance, but that the condition of the respiratory center is best judged by the depth of respiratory movements. Therefore, during administration of the drugs, careful notes should be made regarding this point, especial attention being paid to the freedom of abdominal movements, the factor of chief value in determining respiratory depth. Any evidence that depth is not increasing with slowing of the rate should be taken as an indication to withhold the drugs.

(*c*) *Oxygen-inhalation.*—After respiratory insufficiency has become established, another measure often resorted to, but concerning the value of which there has been uncertainty, is the *inhalation of oxygen*. A patient with slight respiratory insufficiency was given *O* during a period of five minutes. Preceding, during, and following its administration, several observations on systolic blood-pressure were made and averaged. During the inhalation, a fall of 17 mm. Hg. was noted, but the pressure rose quickly to the starting point after the administration was discontinued. Another similar case exhibited the same phenomena, the fall of pressure being only 12 mm. Hg. (Chart VIII). In a third case, the fall was only 7 mm. Hg. No change in pressure was observed during observations on patients suffering no respiratory insufficiency.

Though physiology has shown that an increase of atmospheric *O*-tension above 13 volume per cent, with normal respiration, causes no increase of *O*-absorption by blood, still the phenomena are easily accounted for when it is borne in mind that in respiratory insufficiency alveolar *O*-tension is less than that produced by the above conditions. The deficient alveolar *O*-tension was increased, of course, by an increase in the quantity of atmospheric *O*. Consequently, *O*-absorption, also, was increased, asphyxial stimulation partially eliminated, and blood-pressure fell. Further effects of *O-inhalation* in insufficiency are partial clearing of cyanosis, slight slowing of the respiratory rate, and deepening of the movements. There is every evidence that the condition is partially relieved. But, following its withdrawal, insufficiency is quickly re-

established, for not only does blood-pressure rise, but cyanosis reappears, and the rate and depth of respiration return to the original point. Furthermore, it has been shown that *O* at a greater tension than normal in the atmosphere acts as an irritant upon the air passages, and that at a tension of 80 volume per cent it can produce inflammation. Considering that the air passages are in an inflamed condition already, the continuous *inhalation of O* would probably be harmful. Even during five-minute periods of administration, there is observed, almost constantly, increased restlessness on the part of the patient, who makes frequent efforts to withdraw from the *O*-cup. It is probable, then, that the partial relief of insufficiency during brief administrations is counterbalanced, at least, by the restlessness and discomfort induced, and it may be that the inflamed condition of the lungs is exaggerated by the slight irritation. Relief is partial at best, for insufficiency is due as much to accumulation of CO_2 as to deficiency of *O* in the blood, and *O-inhalation* has no tendency to increase CO_2-elimination. The weight of evidence, then, seems to point towards the probability that the measure is a useless one, at best, and may be actually harmful.

Circulation.—The circulatory condition is indirectly and favorably influenced by measures adapted to meet general and respiratory indications, and in such measures are to be placed greatest dependence. Agents used for their direct action upon the circulation are sedatives, *alcohol,* and stimulants.

(*a*) *Sedatives.*—Of *circulatory sedatives,* most important are *aconite, veratrum, hydrocyanic acid,* and the *nitrites,* all of which are known to be dangerous drugs, and with none of which have I made special observations. The sedative action of the first three, however, consists in slowing of the heart-rate through stimulation of the cardio-inhibitory center (Cushny). But all have a stimulating action upon other portions, also, of the central nervous system, excepting, perhaps, *aconite* and *veratrum* on the respiratory center, upon which their action is not understood. Furthermore, it is doubtful if stimulation of the cardio-inhibitory center by medicinal doses of these drugs would have any effect whatever upon pulse-rate in pneumonia. Stimulation of the center strong enough to overcome the excitation of the heart muscle and accelerator center would require, probably, doses of the drugs too large to be used with safety. For these reasons, all three of the drugs would be contra-indicated, a priori, in the disease.

The *nitrites* are the safest of the sedatives, and, since they act by dilating the peripheral vessels, thus lowering blood-pressure, their administration should cause a decrease in the heart's work. It is possible, therefore, that they may be of some value in preventing overwork of the heart muscle, and thus of aid in preserving the integrity of the circulation.

(*b*) *Alcohol.*—The action of *alcohol* is a matter of too great dispute to warrant its classification as either sedative or stimulant, nor would one be justified in making any dogmatic statement as to its indication. In cases having alcoholic histories and presenting the alcoholic type of the disease, it would seem reasonable to continue, as far as possible, customary conditions under which the tissues have worked. In other cases, experience has led many observers to believe that alcohol is of benefit in pneumonia; others, to the contrary view. Though I have used it and seen it used frequently, sometimes in large quantities, I have not yet made special observations on variations of respiration, pulse- and blood-pressure due to its administration, but I have never seen results, either good or bad, that I could attribute directly to its action. Abel states that moderate quantities, introduced into the circulation with the avoidance of local irritation, have no effect upon heart, blood-vessels, or blood-pressure; in larger quantities, when there is a variation, the pressure is always lowering (7). Cook and Briggs have observed, in the majority of patients in whom no tolerance was established, a slight but transient rise of systolic pressure following its administration, a phenomenon which they attribute to local irritation; and then a distinct fall of pressure, attributed to a sedative action following absorption (8). Cushny suggests that the showing of respiratory-rate and pulse-rate in fevers is due to its influence in diminishing cerebral excitement through its narcotic action. The probability is, therefore, that its administration may lessen cardiac work and nervous irritability and be of benefit during the stages of excitement. But, when enfeeblement of the respiratory or circulatory mechanisms has begun, it is probably contra-indicated. As a conservator of tissue, it is not specially indicated, since food is usually taken well, digestion is not greatly impaired, and natural products for combustion are supplied.

(*c*) *Stimulants.*—It need scarcely be argued that circulatory stimulants are contra-indicated as long as there is no insufficiency. When that condition is established, however, unless it can be relieved, it leads, presumably, to accumulation of the toxic agent, and tends towards a premature, fatal termination. The condition, it has been pointed out, is indicated by low systolic blood-pressure associated with one or more of three conditions, namely, respiratory insufficiency, a small urinary output, and signs of oncoming œdema of the lungs. In combating circulatory insufficiency it is desirable to use some remedy that will have no deleterious effect upon the central nervous system, stimulation of which, especially of the respiratory center, is to be avoided. This is difficult, for *strychnine, caffeine,* and *cocaine* owe their action upon the circulation to stimulation of the nervous system, and even members of the *digitalis* series, whose chief action is upon the cardio-vascular musculature, act as stimulants upon certain centers in the medulla. The last, however, have practically no action upon the respiratory center, and their action upon other portions of the nervous system, excepting the cardio-inhibitory and vaso-constrictor centers, is insignificant. Therefore, members of this series seem to come nearest to fulfilling the requirements, and of these the *tincture of digitalis* is probably the most reliable and efficient.

In the case represented by Chart IX, low systolic blood-

pressure was associated with both respiratory insufficiency and small urinary output, and the lungs were full of loud ronchi. During days 4, 5, and 6, *strychnine* in fairly large doses and *digitaline* (Merck's) were administered hypodermically every four hours with no rise of pressure and no relief. On the night of day 6, *digitaline* was discontinued, the dose of *strychnine* reduced, and *tincture of digitalis* ordered every four hours. Improvement of the cardio-vascular musculature was so great that, after three doses, blood-pressure rose from 105 to 150 mm. Hg. During exhibition of the drug, the urinary output was greatly increased[5] (a certain portion of the 1720 cc. of day 6 was voided during the night and after administration of the drug was begun), and by morning of day 8 the condition of the patient was improved in every respect. Blood-pressure fell, due to less intense asphyxial stimulation, before *digitalis* was discontinued, and for several days thereafter it ranged a little above normal.

Chart X represents a case in which low systolic blood-pressure was associated with a small urinary output. Apparently there occurred an accumulation of the toxic agent which was evidenced by the onset of respiratory insufficiency and acceleration of the pulse-rate. The *tincture of digitalis* was administered every four hours during days 7 and 8, and discontinued on the morning of day 9. During days 7 and 8, before asphyxial stimulation occurred, digitalis exerted but little influence upon blood-pressure, but when respiratory insufficiency became established (day 9), cardio-vascular response was immediate and blood-pressure rose rapidly. This was due, probably, to an improved condition of the cardio-vascular musculature resulting from the action of *digitalis*. Previous impairment was indicated by the otherwise unaccountable fall of pressure preceding the commencement of its administration. In this case, also, after one day of high blood-pressure, there was great improvement in every respect in the patient's condition.[6]

The view may be held that in both of these cases the unto-

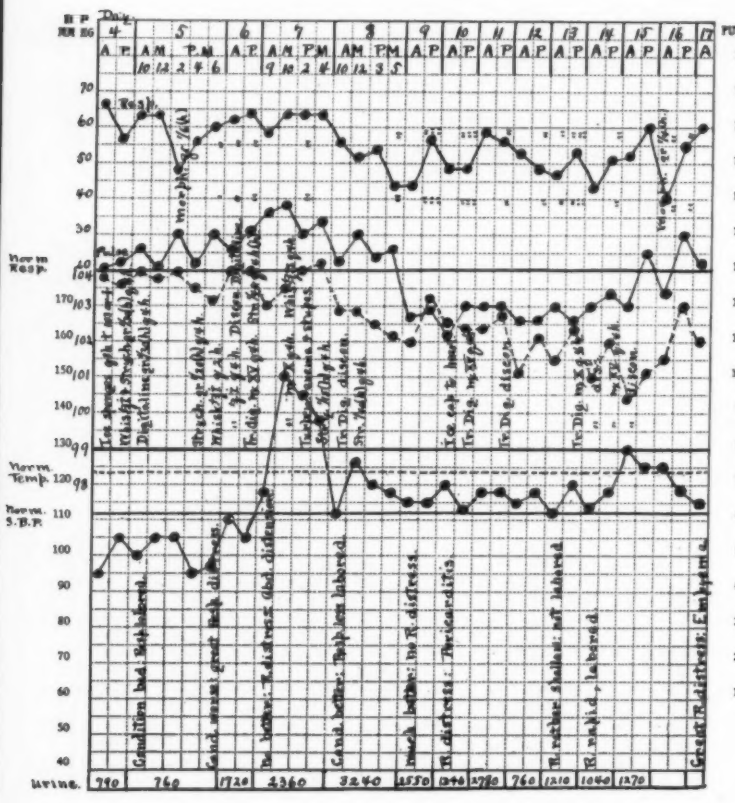

CHART IX.—Watkins, male, colored, age 16, recovery from acute illness, death from complications, empyema, and pericarditis.

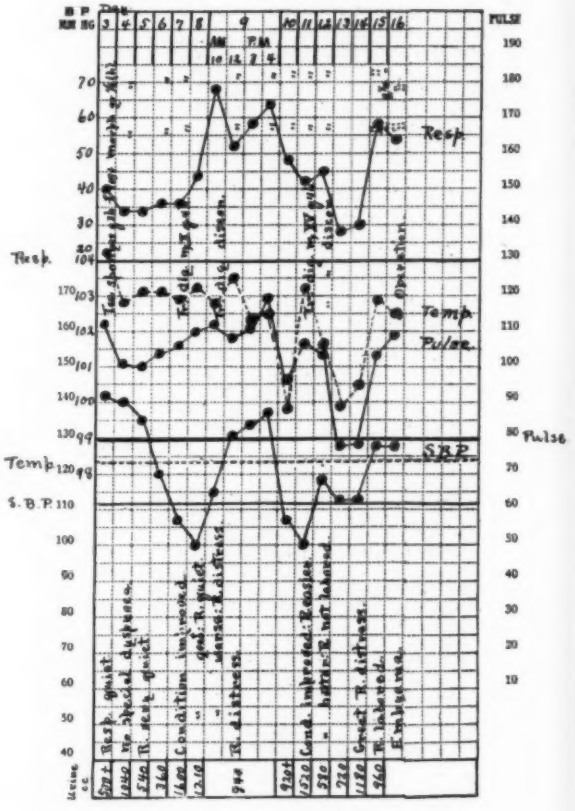

CHART X.—Clark, male, age 28, empyema, recovery.

[5] Erlanger and Hooker have shown that the urinary output bears no relation to variations in blood-pressure, but that it tends to vary with pulse-pressure (3). Unfortunately, no record of diastolic pressure was made, so that the effect of *digitalis* on pulse-pressure is unknown in the case. Previous to its administration the pulse was thready in character, and it is probable that *digitalis* exerted its beneficial influence by increasing pulse-pressure.

[6] The urinary measurements are probably incorrect in this chart. A different result would certainly be anticipated during a period of improvement, and the figures here show a wide variation from those under all similar conditions in the other charts.

ward phenomena immediately following the administration of *digitalis* were due to the action of the drug. But digitalis exerts no such influence upon respiratory-rate or pulse-rate as that represented in the charts. Furthermore, in Chart IX great improvement occurred before *digitalis* was discontinued; and in Chart X, it is shown that administration of the drug in even larger doses under different conditions (days 11, 12) was associated with no similar phenomena, but with slighter rise of blood-pressure and marked lessening of the respiratory-rate and pulse-rate (day 13). The evidence, though very incomplete, seems to be in favor of the view that *digitalis* improved the circulatory condition, and thus aided efficiently in the elimination of the toxic agent, and, possibly, in its destruction through improved metabolism.

Résumé.

I. *Action of the toxic agent of lobar pneumonia.*
   1. Phenomena of the mild action bear the features of stimulation of the central nervous system and cardiac muscles.
   2. Phenomena of severe intoxication appear to result from intensified stimulation, or enfeeblement and exhaustion from overstimulation.
   3. Death occurs from (1) respiratory insufficiency terminating in asphyxiation or in exhaustion of the respiratory center, or (2) circulatory insufficiency, which leads, presumably, to accumulation of the toxic agent, and which may induce œdema of the lungs or end in exhaustion of the heart muscle.

II. *Therapeutics.*
   1. Elimination of the toxic agent.—*Internal hydrotherapy.*
   2. Amelioration of harmful influences.
      a. Fever—*external hydrotherapy;* pain—*ice bag and analgesics;* restlessness, insomnia, delirium—*external hydrotherapy, analgesics, and narcotics.*
      b. Respiratory indications.
         (1) *Heroin* or *morphine* every two hours for a respiratory-rate of 36 or greater.
         (2) *O-inhalation* is probably useless and may be harmful.
      c. Circulatory indications.
         (1) Circulatory sedatives probably contra-indicated, excepting the *nitrates,* which may be of benefit during early periods of increased cardiac work.
         (2) Alcohol indicated in alcoholic cases; may be of benefit when there is no circulatory insufficiency.
         (3) Circulatory stimulants contra-indicated, except members of the *digitalis* series. The indication is low blood-pressure associated with one or more of three conditions, namely, respiratory insufficiency, small urinary output, œdema of lungs.

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A CASE OF UNUSUALLY LARGE AORTIC ANEURYSM.[1]

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The aneurysm here reported is regarded as worthy of record, chiefly on acount of its enormous size and the presence of a collateral venous circulation.

Mr. F. R., age 60; admitted December 6, 1893; occupation, soldier; nationality, Germany.

Previous History.—No reliable family history of the patient's early life was obtained; also no history of syphilis. Patient stated that since he left the army he had been employed as a baker, and that he used to exert himself considerably at times lifting barrels of flour. He never, however, noticed any bad effects from it. Admission certificate states that he suffered with rheumatism for about three years previous to admission. He was first admitted December 6, 1893, suffering with a chronic form of mental trouble, and was discharged December 5, 1894—improved. He was re-admitted April 19, 1895 from the Central Branch, N. H. D. V. S., suffering with a recurrent attack of the same men-

[1] Presented by invitation before the Medical Society of the District of Columbia, April 26, 1905.

tal trouble. At this time the patient was a strong robust man, and showed no evidence whatever of physical debility. He remained in one of the chronic wards in good physical condition until the spring of 1903. During this period his mental condition alternated between excitement and depression, but he was never restrained or confined to bed, and at times was well enough to be given parole about the grounds.

On April 2, 1903, patient was transferred to the hospital ward, complaining of pain in the chest. This pain seemed to be worse at night, and interfered considerably with his sleep. It also aggravated his mental trouble, as he labored under the delusion that his pursuers were pumping gas into his chest. His condition remained practically unchanged until later in the summer of 1903 when in addition to the pain there was a slight cough and dyspnea, with some harshness of the voice. There appeared during September slight swelling near the right border of the sternum between the 2d and 4th costal cartilages. This pulsating expansile tumor gradually increased in size so that on November 1, 1903, it was about the size of a small lemon. It continued to grow, but the symptoms remained about the same until the spring of 1904, when they became more pronounced.

The following notes were made June 11, 1904, when the case was first seen by the writer:

Inspection.—There is a pulsating tumor 9 cm. in diameter projecting from the chest wall 6 cm. situated to the right of the mid-sternal line between the 2d and 5th costal cartilages, and extending to the right nearly as far as the nipple line. The skin over the tumor is thin, shiny and tense. There is no pulsation of the vessels of the neck, no evidence of venous compression, nor of irritation of the sympathetic; the pupils being equal, of medium size, and react readily to light. The apex beat is seen faintly in the 5th interspace 1 cm. to the left of the nipple line. There is clubbing of the fingers and slight incurving of the nails.

On *palpation* there is felt over the tumor a forcible expansile impulse of considerable resistance. There is a marked diastolic shock and systolic impulse. The apex beat is feeble.

Percussion.—Area of cardiac dullness is slightly increased. The note over the tumor and for a small area surrounding it is flat. This flatness blends with the cardiac dullness to the left.

On *auscultation* no bruit can be heard. The only adventitious sound present is a loud creaking sound heard on inspiration in the right infraclavicular space. There are no valvular murmurs, but the second aortic sound is markedly accentuated. About every 15 or 20 beats there is absence of the first sound. There is no appreciable difference in time between the right and left radial pulses, but the right is very much weaker than the left. There is no tracheal tugging.

The patient complains of continued dull pain, with occasional sharp lancinating attacks felt most distinctly in the right axilla and along the right arm. There is occasional slight cough, considerable dyspnea, and the voice is quite husky. As near as can be made out the 3d and 4th costal cartilages are eroded, as well as a few cm. of the 3d and 4th ribs.

The tumor from about this time increased in size with remarkable rapidity. There was noticed about August 1, 1904, enlargement of the superficial veins of the right half of the body. These veins rapidly became more dilated and tortuous, the flow being from above downward. The veins entering into this collateral circulation, were in the order of their size, the right superficial epigastric, a large branch from the left superficial epigastric joining it near the umbilicus, several lateral thoracic veins, the right jugular and a network of superficial veins over the tumor, and over the superior and anterior surfaces of the right shoulder. This collateral venous circulation was thought to be due to pressure on the right innominate vein, and perhaps also slightly on the superior vena cava.

There appeared during September, in addition to the symptoms above mentioned, well marked tracheal tugging, and also an area of softening about 5 cm. in diameter at the summit of the tumor. This area was discolored, but at no time was there any weeping or leakage of blood.

The dyspnea and pain became quite distressing during October, and on the 23d of that month a sudden change occurred. The dyspnea became markedly increased, the extremities were cyanosed, the temperature rose from normal to 100 degrees, pulse from 82 to 110 and quite feeble, and the respiration from 22 to 28 per minute. The next day this condition was somewhat improved, but he gradually grew weaker during the succeeding 21 days and death occurred November 13, 1904, at 8:58 a. m. For a few minutes preceding death the pulse fell to 13 and the respiration to 4 per minute.

AUTOPSY NOTES.—(Case came to autopsy in the service of Dr. I. W. Blackburn.)

Autopsy performed at 1.50 p. m., November 13, 1904, five hours after death. The body is that of a medium size, well built, and well nourished white man. It is slightly warm, and there is no post-mortem rigidity, and very slight cadaveric lividity. The pupils are equal. There are no scars on the genital organs or elsewhere. The superficial veins of the right half of the trunk are somewhat dilated and tortuous, especially the right superficial epigastric. There is a tumor of the following dimensions occupying the space between the mid-sternal line and the axilla, and the 2d and 7th ribs on the right side, H 30 cm., V 23¾ cm., C 65 cm. The skin over the tumor is smooth and shiny. It is somewhat soft to the touch over its entire extent, but more markedly so over an area about 5 cm. in diameter at the summit. There is some edema of the right arm and tissues adjacent to the tumor.

The aneurysm with heart, lungs, and a large portion of chest wall are removed en masse by the following incisions: an incision in the left mammary line extending from the clavicle to the costal margin; another the entire length of the right posterior axillary line—their ends being joined by an incision along the costal margin, and one along the superior opening of the thorax —the sternal ends of the clavicles being disarticulated.

Fluid blood flows freely from the great vessels.

Pericardium.—There are many old fibrous adhesions between the pericardium and pleura; otherwise it appears normal.

Heart and Aneurysm.—There is apparently no cardiac hypertrophy. In order to preserve the specimen intact the heart is not detached, but the aortic arch is opened by an incision begin-

FIG. 1.—Taken 5½ months before death.

FIG. 3.—Taken the day before death.

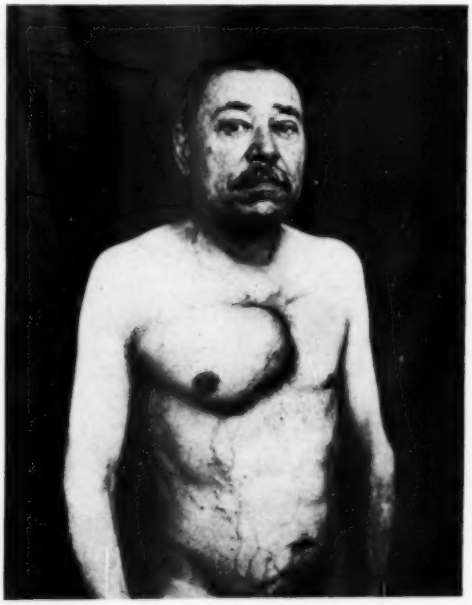

FIG. 2.—Taken 45 days before death, showing collateral circulation.

FIG. 4.—Taken the day before death, showing the lateral extent of the aneurysm and the area of softening of the skin over the most prominent point.

ning just above the valves at the anterior-left-lateral border and keeping this same relation all the way around. The aortic arch is much dilated and shows numerous atheromatous patches; many of the calcareous plates protrude into the lumen of the vessel. The greatest dilatation is between the valves and the origin of the innominate artery and is large enough to readily admit the closed fist. Through the right wall of this sac is an oval opening 8 cm. in its long diameter, its lower margin being 6 cm. above the aortic valve. This opens into an enormous sac which occupies the greater part of the right half of the chest. This sac is opened, after the adherent right lung is dissected away, by an incision along its posterior superior border. This sac contains, after the fluid blood is drained off, 2200 grams of clot. 1520 grams of this is from the extra-thoracic portion of the sac, and is light brown in color, rather firm, laminated and adherent to the sac wall. The remaining 680 grams from the intra-thoracic portion of the sac is more recent, darker and quite soft. The intra-thoracic portion of the sac is not nearly filled with clot, as it was from this part that most of the fluid blood escaped. There is seen an area of atrophy of the sac wall about 6 cm. in diameter at the posterior-superior portion near the median line. This had permitted oozing of blood into the anterior-inferior portion of the upper lobe of the right lung, and the formation at this point of a clot about the size of a small lemon.

The sac protrudes through the chest wall between the 3d and 5th ribs. The 3d rib is eroded along its inferior border about ⅓ of its width, beginning 7½ cm. from the edge of the sternum. The 4th rib is completely eroded for a distance of 12 cm., beginning 6¾ cm. from the edge of the sternum. An irregular fragment of this rib 6 cm. in length is found loose in the extra-thoracic sac. The cartilage of the 5th rib is broken 2½ cm. from the sternum, and the rib is displaced forward and slightly downward. Its superior border is eroded to about the same extent as is the inferior border of the 3d, beginning the same distance from the sternum. This opening measures H 12 cm., V 9 cm. The aortic valves are slightly thickened, but not calcareous and appear to be competent. The other valves, the coronaries and myocardium, are not examined as it is desired to preserve the specimen intact. The lower portion of the thoracic, aorta, and the abdominal aorta show nothing abnormal.

Pleuræ.—The pleuræ are thickened, and there are numerous fibrous adhesions between them and the pericardium and diaphragm.

Lungs.—These organs are necessarily much mutilated in removal. The left lung is œdematous, but shows no other abnormality. The right lung shows marked compression, and the clot mentioned above.

Spleen.—200 grams; abnormally firm and full of blood.

Kidneys.—170 grams each. Capsules are readily removed; the surfaces are a little glandular.

Liver.—1390 grams; apparently normal. Gall-bladder contains 40 cc. of orange-colored bile.

Intestines.—Excepting a constriction in the sigmoid flexure admitting only the index finger, the intestines appear normal.

Pancreas.—Apparently normal.

Brain.—1100 grams. The membranes show considerable opacity and there is general shrinkage of the convolutions. The vessels show little patches of opacity, but no calcareous change. Otherwise there is nothing abnormal to be noted.

Skull.—Rather thin. Frontal suture is persistent.

Autopsy closed at 4 p. m.

Adopting the view that a true aneurysm is one consisting of one or more of the coats of the vessel, it is difficult to say just how much of this aneurysm is true and how much false. We can state with a fair degree of certainty that the intima and media ended at the opening in the dilated aortic arch, and that the adventitia became very much distended. It was impossible to determine the extent of this distention, owing to the new formation of fibrous tissue, but it is hardly likely that it extended beyond the opening in the chest wall. Perhaps the greatest pressure on the sac was exerted at this point and produced rupture of the adventitia. This supposition would make all of the extra-thoracic portion of the sac purely false.

It is difficult to demonstrate, without serious injury to the specimen, the exact site of venous compression which produced the collateral circulation. Apparently the greatest pressure was exerted on the superior vena cava and the right innominate vein was probably pressed upward against the clavicle. Another possible explanation of obstruction to the flow of blood in the innominate vein is that, as the superior vena cava was pressed toward the left, it may have caused some angulation of the innominate.

The cause of the sudden change in the patient's condition on October 23 was thought to be due to the hemorrhage into the right lung.

Another point of interest in this case is the influence the physical disease appeared to have upon the mental condition. Although the patient was adjudged to be of unsound mind for a period of nearly ten years, there is no history of such well marked delusions and such vivid hallucinations as were manifest during the last seven or eight months of his life. Every morning he would complain of the way "they" treated him during the night with their electric wires and gas pipes. He believed that they pumped gas into his chest, and that this accounted for the swelling, pain, and difficulty in breathing. He begged to have the tumor opened to let the gas out, or to have a poultice applied, or a salve or leeches put on. He threatened to open it himself, and had to be closely guarded to prevent such threats from being carried into execution. The hallucinations were entirely auditory. He would hear the voices of his persecutors day and night, and would scream back in answer to them, using much profanity and abuse.

These mental symptoms grew more and more pronounced until within about three weeks of his death when they subsided somewhat. They were, however, well marked even to the end, but owing to his weak and exhausted condition they were not so apparent, as he could no longer jump out of bed, nor talk so loud as he had done previously. The patient manifested no other mental symptoms of interest. There was a fairly well marked degree of dementia.

We see therefore a connection between the mental symptoms and the physical disease, reminding us of cases occasionally met with in the literature of misinterpreted sensations and other mental phenomena occurring in various visceral diseases. I refer particularly to the observations of Dr. Henry Head, Brain, 1901, and Dr. Carey B. Gamble, Johns Hopkins Bulletin, July and August, 1904.

I wish to state that I am indebted to Dr. I. W. Blackburn for useful suggestions and supervision of the preparation of the specimen, and to Dr. H. J. Nichols for assistance with the making of a plaster cast and the photographs.

ACUTE PERICARDITIS COMPLICATING ACUTE LOBAR PNEUMONIA.[1]

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During the period of sixteen years, viz. from May 15, 1889, to May 15, 1905, 665 patients suffering from acute lobar pneumonia have been admitted to the Johns Hopkins Hospital. These figures include all cases, both those admitted with the disease and those developing terminal pneumonias.

Acute pericarditis was present in 31 patients, or 4.66 per cent. In 13 or 41.9 per cent, pericarditis was recognized during life; in the remaining 18 patients it was only recognized at autopsy. Autopsies made in 26 instances confirmed the diagnosis of acute pericarditis or showed its presence when not suspected before death. The analysis of the cases is as follows:

Age.—The average age of the patients was 32.5 years. The complication occurs more frequently in young adults, only 5 patients out of the last 19 in this series being above the average age (32.5 years) and the majority were much younger.

Sex.—There were 22 males and 9 females. Of the males 10 were white and 12 colored; among the females 5 were white and 4 were colored.

Duration.—The duration of the illness being so indefinite and in many cases unobtainable, I have merely considered the time the patient was in the hospital, which in most instances was quite short. In 2 patients, however, it was long, due to a protracted illness of another nature (arthritis deformans and typhoid fever) in a third patient the development of an empyema caused much prolongation of the disease. The remaining 28 patients showed an average duration of 6 days.

Lung Involvement.—The portions of the lungs involved during the disease were as follows:

Right side	Times	Left side	Times
Upper lobe	2	Upper lobe	0
Lower lobe	1	Lower lobe	2
Upper and middle lobes	2	.....	..
Upper and lower lobes	2	.....	..
Middle and lower lobes	1	.....	..
All lobes	5	Both lobes	3
Total	13	Total	5

The lungs on both sides of the chest were involved at the same time in 13 patients, the distribution of consolidation being as follows:

Right side	Left side	Times
Right lower lobe	and left lower lobe	2
All lobes	and left lower lobe	3
Right lower	and left upper and lower lobe	2
Right lower	and middle and left upper lobe	1
Right lower	and middle and left lower lobe	1
Right upper	and lower and left lower lobe	1
Right upper	and lower and left upper and lower lobe	1
Right upper	and left lower lobe	1
Right upper	and left upper and lower lobe	1
Total		13

Heart condition.—In regard to the recognition of the pericarditis during life it may be said that in 12 instances there was no note of any pericardial rub, or other symptoms to indicate a pericarditis. In 13 patients pericarditis was diagnosed. Five cases were doubtful; in one the patient was too restless and delirious for a satisfactory examination. Of the remaining four, the sounds in the lungs were so loud, that the heart condition was masked, though in one instance a suspicious rub was heard over the heart, but it was not sufficiently plain to justify a diagnosis of pericarditis. In the sixth doubtful case there was no note of any pericardial rub, but the increase of cardiac dullness to the right of the sternum was suggestive of an effusion into the pericardium and the autopsy in this case showed some excess of fluid.

Complications.—In the clinical histories pleurisy was by far the most common complication, occurring as follows:

Acute fibrinous pleurisy, right side, 7 cases; left side, 7 cases; both sides, 2 cases; pleurisy with effusion; right side, 1 case; left side, 1 case. The other complications were empyema 3 times; acute nephritis, acute endocarditis, and pneumothorax once each. Of the associated diseases, typhoid fever, arthritis deformans and acute articular rheumatism occurred once each, the pneumonia having developed during their course.

Mortality.—The mortality was extremely high, 29 patients out of the 31 dying, or about 93.5 per cent.

Remarks.—A marked history of alcoholism was given by 10 patients. Occupation had little bearing on the disease, the majority being laborers as in most hospital series. Two patients gave a history of previous attacks of pneumonia. Another had had both pneumonia and acute rheumatic fever previously and one other acute rheumatic fever only. Two patients showed a general pneumococcus infection, the organism being cultivated from the blood during life. Four cases were admitted in active delirium and two became delirious during the course of the disease—delirium therefore occurring in 19.3 per cent. There were two instances of terminal

[1] Read before the Johns Hopkins Hospital Medical Society, June 5, 1905.

pneumonia or 6.45 per cent. This small percentage is rather interesting as we know what a fatal complication pericarditis is and how often it is a feature of terminal infections in other cases. It does not seem so common in terminal pneumonia, judging from the small number of cases found here.

The Autopsy Records.—As so many of the fatal cases come to autopsy, their pathological and bacteriological findings should be reviewed, especially because in many no definite diagnosis could be made before death. During the past sixteen years 184 autopsies have been made at the hospital on cases of acute lobar pneumonia; among these there were 29 cases, or 15.7% with acute pericarditis, 26 of which are noted above, the other three having no clinical histories.

Lung Involvement.—In analysing these cases we find the lung involved as follows, according to lobes consolidated:

Right side	Times	Left side	Times
Right upper	2	Left upper	0
Right lower	1	Left lower	2
Right upper and lower	1		
Right upper and middle	2		
Right lower and middle	1		
All lobes	7	Both lobes	2
Total	14	Total	4

In combination both sides of the chest were involved together in 11 cases as follows:

Right side	Left side	Times
Right upper and	left lower	2
Right upper and	both left lobes	2
All right lobes and	left lower	2
All right lobes and	both left lobes	1
Right middle and lower and	left lower	1
Right middle and lower and	left upper	1
Right upper and lower and	left upper and lower	1
Right lower and	left lower	1
		11

Pericarditis.—The varieties of pericarditis were as follows in order of frequency.

Acute fibrino-purulent pericarditis	10 times.
Acute sero-fibrinous pericarditis	9 "
Acute fibrinous pericarditis	8 "
Acute purulent pericarditis	2 "

In 3 instances only, was a very large amount of fluid present. In two patients, one with 500 cc. and the other with 800 cc. of fluid, the clinical history was not obtainable, so the question as to whether the pericardial effusion was diagnosed before death cannot be answered. The third patient had 1000 cc. of fluid, but the associated empyema on the left side interfered with the recognition of the pericardial effusion and it was only discovered at autopsy.

Bacteriology.—In regard to the organisms cultivated and recognized, the presence of the pneumococcus only, when found, is tabulated, thus:

Lungs.—The pneumococcus was obtained in culture in 16 instances and found microscopically in cover-slip smears made at autopsy 7 times when the cultures were negative, a total of 23 in 29 autopsies. From the *pericardium* the pneumococcus was cultivated 12 times and the smears showed its presence in 7 other cases. Consequently, in 19 of the 29 cases of pericarditis the pneumococcus was the organism present. No other important organisms were cultivated, in most instances the cultures or smears being sterile or contaminated.

Bacteriological findings elsewhere in the body were as follows:

Heart's blood pneumococcus cultivated	5 times.
Pleural exudate pneumococcus cultivated	3 "
Empyema pneumococcus cultivated	2 "
Lung abscess pneumococcus cultivated	2 "
Mitral valve pneumococcus cultivated	1 time.
Brain pneumococcus cultivated	1 "

Complications.—Pleurisy was so frequent as to be regarded as more than a complication, being present in 28 of the 29 autopsies. The sides involved were as follows: right side, 13 times alone; left side, 8 times alone; both sides at same time in 7 instances. Pleurisy with effusion occurred 12 times. Empyema was found 3 times, twice on the right side, both of them being encapsulated between the diaphragm and lungs. In the third case the empyema was on the left side, not encapsulated. Abscess of the lung occurred twice and acute purulent meningitis and acute mitral endocarditis once each. Acute mediastinitis was present in a number of cases, its frequency being hard to determine exactly, as often no note of its presence or absence was given in the records.

Remarks.—In looking over both the clinical and pathological records, one is especially struck with the seriousness of pericarditis in acute lobar pneumonia. It is hard to say whether the cases of pneumonia, in which pericarditis occurred, were any more severe than usual or whether pericarditis is only one of the many manifestations which develop at the end of a severe pneumonia. A striking fact in the records is the more frequent involvement of the lung and pleura on the right side. This would seem to indicate that pericarditis is due to a metastatic process, through the blood or lymphatics rather than by direct extension from the lung or pleura. This is of interest in the light of the fact that great stress has been laid by many in previous reports on the synchronous involvement of the left lung and pleura, which as we know envelops the heart more than on the right side.

In the autopsy records, I found a case of a woman who had a large hemorrhagic infarct in the upper right lobe of her lung, the pleural surfaces over this area showing fresh fibrinous adhesions; a fresh sero-fibrinous pericarditis was also present. The lung and pleura were otherwise not involved, yet the cultures from the infarct and pericardium showed the presence of the pneumococcus. This case seems strongly to favor the view of an infection by the blood stream or lymphatics rather than by direct extension.

Recent work also shows how often the pneumococcus can be cultivated from the circulation, or other pneumococcic processes outside of the lung involved. The great frequency of pleurisy may be of some importance in explaining the extension of the disease, but granting this, the right side has

been found involved more than the left, the pleural surface of which (*i. e.* left) is much more in contact with the pericardium.

The prognosis of pericarditis complicating acute pneumonia, to judge from our own cases and the general statistics in the literature, is exceedingly grave. Our two cases of recovery were of interest, owing to the fact that both were associated with another disease; one, a white male, age 43 years, who was admitted for treatment of arthritis deformans and spondylitis, was in the hospital 237 days. After admission he had pneumonia involving the right and left lower lobes lasting several weeks; during its course a definite pericardial rub was heard for several days. There was no active arthritis at any time to suggest a rheumatic pericarditis; later the patient left the hospital much improved. The other instance of recovery was a white female, age 29 years, who was admitted with all the signs of pneumonia, with involvement of the right upper and lower and left lower lobes. A pericardial rub was present on admission and lasted several days. Later the patient had an attack of fever, with positive Widal reaction, rose spots, and an enlarged spleen; after remaining in the hospital 119 days she was discharged quite well.

The treatment of patients in whom the pericardial rub was recognized during life, was of the general supportive character, usually employed in pericarditis. Locally ice-bags and blistering were tried. All treatment except in the cases of two who recovered seemed to be unavailing.

In no instances was aspiration or free drainage tried.

Literature.—Upon a review of the literature bearing on pericarditis as a complication of pneumonia, opinions are found to vary somewhat as regards its frequency, mode of infection and mortality. Most writers however agree as to its seriousness, thus:

Fowler and Godlee[1] found pericarditis 17 times in 128 fatal cases of pneumonia or 13.2%. They say: "It is generally stated that this complication (pericarditis) is more frequent in cases of pneumonia in which a portion of the left lung in contact with the pericardium is consolidated, but in these fatal cases the right lung was involved 10 times, the left 6, and both lungs once."

Our statistics seem to agree quite closely with theirs.

Pye-Smith[2] says: "Pericarditis is not infrequent and is an extremely dangerous complication. Double pneumonia with pericarditis is almost invariably fatal. * * * "Pericarditis follows more particularly when the pneumonia or pleurisy is on the left side. In 434 cases of pneumonia, pericarditis was present in 14, all fatal."

A. H. Smith[3] says: "This complication (pericarditis) occurs in 2 to 8% of the cases of pneumonia, according to different authorities. At the Presbyterian Hospital, N. Y., it was made out during life in 6 out of 485 cases of pneumonia, about 1.2%."

Strümpell[4] in speaking of the complications of pneumonia, after mentioning pleurisy, says: "Still worse is a sero-fibrinous or purulent pericarditis, which in not very rare instances, is revealed at autopsy as the special cause of death. We must note however that recovery sometimes takes place in spite of an empyema or a purulent pericarditis."

Osler[5] found pericarditis present in 5 of his 100 autopsies.

In their book on Pneumonia, *Sturges and Coupland*[6] say: "Pericarditis is an interesting and serious complication and in many instances its presence is not declared during life. It is mostly described as more common in association with pneumonia and pleurisy of the left side (this statement made on the authority of Bouillard) and hence may be regarded as due to a direct extension of the inflammatory process to the pericardium. But in an analysis of 144 autopsies (Middlesex Hospital, 1873-1889) this is by no means the rule, for out of 24 cases of acute pericarditis, in no fewer than 11 was the right lung involved, in 10 the left and in 3 both lungs. It may be remembered however that pericarditis was more frequently combined with pleurisy of the left side."

"In 23 cases of pericarditis and pneumonia coexisting, the right lung was consolidated in 16 either solely, which was the rule or with very slight consolidation of the left; of the remaining 7 cases, 4 were not distinctive." Among some statistics they quote are the following: "Leudet met 6 cases of pericarditis out of 83 pneumonias. Austin Flint 8 out of 133 cases. Behier 3 out of 114 cases of pneumonia. Huss in his 2616 cases of pneumonia gives 22 cases of pericarditis, 12 of which were fatal."

Babcock[7] says: "Acute lobar pneumonia should certainly be given a place only subordinate to acute articular rheumatism, in the etiology of pericarditis." He quotes Preble as having found pericarditis in 92.4% of 79 fatal cases of pneumonia collected from the post-mortem records of the Cook County Hospital, Chicago. Preble came to the conclusion that the danger of pericarditis bears a distinct relation to the extent of lung involvement and is also more frequent in left than right-sided pneumonias.

McCrae, Fyshe and *Ainley*[8] in an analysis of 486 cases of pneumonia and 100 autopsies, found pericarditis in 11 cases, about 2.3%, (ours 4.66%) whereas the analysis of the autopsies gave a percentage of 17%, (ours 15.7%). "The discrepancy that exists between the clinical and pathological records is easily understood when one remembers the comparatively short time in which a pericardial friction rub may be present and the small amount of fluid present in many cases." "Of their cases 7 occurred with involvement of both lungs, 5 of the right side and 4 of the left."

Anders[9] found acute pericarditis 14 times in 275 cases of pneumonia, about 5%, and *Geo. W. Norris*[10] in 500 cases of pneumonia in the Pennsylvania Hospital (1897-1901), found acute pericarditis as a complication in 4 cases, 3 of which were fatal.

J. A. Scott[11] reports and discusses an interesting case of purulent pericarditis secondary to pneumonia with operation and recovery. In cases where fluid is suspected, free drainage even in desperate cases may give favorable results at times. One of our cases which might have yielded better results with aspiration and free drainage, was the one mentioned with a large pericardial effusion (1000 cc.), but

the accompanying left-sided empyema masked the pericardial condition.

John B. Roberts[31] has an interesting article in the Amer. Jr. Med. Sciences for December, 1897, on the surgical treatment of suppurative pericarditis; and *Morris Manges*[32] says: "There have been 6 cases of pericarditis in the Mt. Sinai Hospital, N. Y., 3 recovered and 3 died. Aspiration did good in all but one case of a boy with double pneumonia and purulent pericarditis, who recovered in 38 days after aspirating, opening and drainage of the pericardium. *Skoda's* two rules for entering the pericardial sac are given: (1) Distension with a large exudate, showing no tendency to absorption and the patient getting worse, and (2) a vital indication is intense dyspnea.

Among the French are found the following statistics:

Netter[33] says: "Lesions of the pericardium are not at all exceptional; they are analogous to those of the pleura with which they often coexist."

"It varies with the different years and the severity of the pneumonia, thus we note its frequency in 1804-05, again in 1837, '76, '82, '86, and 1890. In our series pericarditis was most common in 1900, there being 6 cases. As to statistics, Netter says: "Ormerod found pericarditis 12 times in 100 pneumonias, Leudet 6 in 83 cases and Grissole 3 times in 58 cases of pneumonia."

Vignau[34] collecting and combining various statistics, believes that it occurs in from 5 to 8%.

Laudouzy[35] says: "Pericarditis was observed in 8% of Netter's cases. Rarely is it accompanied by an abundant effusion and coexists often with other pneumococcic manifestations as meningitis, endocarditis, etc." *P. Merklen*[36] says: "Bouillard considers the complication (pericarditis) as common, others only in 1 to 2% of cases."

Among the German statistics, *Sello*[37] reports upon 750 cases of pneumonia, in which he found pericarditis in 7 cases, or about 0.9%; 5 died and 2 recovered. In 4 purulent cases, the right lung was involved in 3 and the left only once. Sello reports other men as finding this complication as follows; von Jürgensen in 0.5%, Fismer in 3.9% and Rychner in 2.7%.

To illustrate the more frequent involvement of the right lung *John L. Steven*[38] found pericarditis 13 times in 120 fatal cases of pneumonia; the right lung being involved in 8 cases. Left in 3 cases and both lungs in 2 cases.

John Hay[39] reports in the Lancet on 200 cases of acute lobar pneumonia. He found 9 cases of pericarditis, 6 of which were fatal; he says: "I found it to be a most serious complication, probably because it is so potent in damaging the myocardium, also from the fact that it is sometimes merely a terminal event in a severe case or again it may be and I believe, is, frequently, a symptom of its severity."

In a report of 28 cases of suppurative pericarditis in children, *George F. Stille*[40] found that 11 gave positive cultures of pneumococci, of the rest, although no bacteriological examination was made of the pericardial fluid, yet the other associated lesions, empyema or pleurisy following a pneumonia, yielded pneumococci.

Sears and Larrabee's report[41] of 949 cases of pneumonia I wish to give somewhat in detail because our observations seem to agree fairly closely with theirs. "The recognized difficulty of diagnosing pericarditis in the presence of pneumonia received a further illustration in these cases, since only about half were discovered during life, and in some of these, which were represented only by a friction rub, the inflammation may have been outside and not within the pericardial sac, yet the number that was found at autopsy, shows that it is not a very rare complication, at least among the fatal cases, since it was found in 8 of 72 autopsies. Out of 19 cases in which it was diagnosed, 11 died; in some of which it was simply an incident in a general pneumococcus septicemia. In 5 only a considerable amount of fluid was present and in 3 was there sufficient to have embarrassed the heart."

"It occurred more frequently when the right lung alone was attacked, for in 10 of 18 cases in which there were complete data, it was confined to that side. The distribution of lung involved being as follows: Right upper, 3 cases; right lower, 2 cases; whole right lung, 3 cases; left upper lobe, 1 case; left lower, 1 case; whole left lung, 1 case. The following combinations of both lungs occurred *once* each whole left lung, with right lower; whole left lung, right middle; whole right lung, with left lower; right upper and lower and left lower; right middle and lower and left lower; right upper and middle, and left lower; and right and left lower once. Acute mediastinitis was found 3 times at autopsy."

Finally *F. P. Henry*[42] reports upon the clinical and pathological findings in a case of pneumonia of the left side with purulent pericarditis and says: "A study of this case has convinced me that the diagnosis of pericardial effusion complicating left-sided pneumonia, is to be made, as much by the symptom, (cyanosis, rapid pulse and dyspnea) as by the physical signs."

Conclusion.—It may be said that pericarditis developing during the course of an acute lobar pneumonia, is a most serious and important complication occurring more especially in young adults, frequently insidious, latent, and often not recognized during life.

It appears to arise as frequently by a metastatic process as by direct extension.

Treatment is very unsatisfactory and often unavailing, except when fluid is present in which case it is more surgical than medical.

In all patients with pneumonia, a most careful watch should be kept on the heart, as this complication appears to be much more frequent than is generally supposed, and urgent treatment in the early stages may materially reduce a high mortality.

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THE RISE OF THE PRESENT CONCEPTIONS AS TO THE CAUSE OF THE HEAT-BEAT.

I. Early Ideas, and the Neurogenic Theory.[1]

By E. G. Martin.

About the middle of the eighteenth century Haller gathered together in his great work, The Elements of Physiology, all the known physiological facts and all the accepted physiological theories of his time. Although his presentation of the various theories was undoubtedly influenced somewhat by his own views, there is no reason to suppose that the thought of his time is not truly represented. All works on general physiology since the time of Haller refer constantly to him, and in the first half of the nineteenth century, particularly, all theoretical points were discussed with reference to his views, either upholding his standpoint or opposing it. For this reason, it seems to me, no better starting point can be found for a review of the growth of a theory in modern times than his work offers. I have chosen, therefore, to begin this study with an account of the facts regarding the heart-beat which were known to Haller, together with his interpretation of them.

In addition to the general facts of the heart's action, which had been known since the time of Harvey, Haller was in possession of a few special facts. These were, first, that the excised heart of a frog continues to beat for a considerable time after removal from the body, second, the results of some experiments performed by himself. In these experiments, performed upon mammals, he cut the venæ cavæ so that no blood could enter the right auricle. He observed that this chamber, thus emptied of blood, promptly ceased to beat, although the other parts of the organ continued to contract as usual. Haller concluded that inasmuch as the heart continues to beat after removal from the body, it must contain within its own substance, independently of its nervous or other connections, the property of irritability. By the term "irritability" Haller meant the ability to respond to stimulation by contraction. He supposed that this property was possessed by the heart to a very high degree, much higher, in fact, than was exhibited by any other of the bodily tissues. He supposed that the heart was excited to contract normally by the blood flowing through it, being led to this conclusion by this observation that a chamber of the heart came to rest when its blood supply was cut off. He thought that in the case of the excised heart of the frog, the stimulus for the long continued activity was furnished by the bubble of air which was enclosed within it. He had made the observation that the inner surface of the muscular wall of the heart is much more sensitive to stimulation than the outer surface.

For more than fifty years after Haller's time, his explanations of the cause of the heart-beat appears to have received general acceptance.

At any rate it was not until the end of the first decade of the nineteenth century that his views were called in question. Physiologists had been sufficiently active in other directions during this half-century, but it was not until the time of which I am speaking that their attention was directed again to this particular field of inquiry. The work which had the effect of exciting interest at this time in the cause of the heart-beat, because of the complete refutation of Haller's views it seemed to contain, was that of the French neurologist and physiologist, Legallois, a brief account of whose life, I wish now to give.

Cesar Julien Jean Legallois was born in a little village of Bretagne in 1770. After completing his elementary studies, he entered upon the study of medicine at Caen. He was still in this place when the Revolution broke out, and when, in 1793, on account of the proscription of the Girondins, the provinces rose in insurrection against the Convention, he joined in the uprising. He was denounced, was obliged to conceal himself, and sought a refuge among the medical students in the Paris hospitals. Here he was found out and denounced a second time. This time, how-

[1] Read before the Physiological Seminary of the Johns Hopkins University, February 24, 1904.

ever, instead of attempting to escape, the young student presented himself before the Committee on saltpeter and gunpowder, submitted to a severe examination, and proved that he could be useful to the Committee. The outcome was that instead of suffering punishment as an insurrectionist, he was sent to his department to direct the manufacture of gunpowder there. Upon the foundation of the School of Hygiene a year later, Legallois was entered as pupil from his district. He distinguished himself at this school, combining the study of medicine with that of ancient and modern languages, and pursuing both with success. He received his doctor's degree in 1801. With the beginning of his active life work as a physician, began also his career as a scientific investigator. During the twelve succeeding years he carried on a number of researches, chiefly upon the functions of the spinal cord. In the year 1813 he was appointed physician at the Bicêtre, a hospital about five miles south of Paris. It was his custom to make the trip each day, between Paris and the hospital, on foot. On one of these journeys he contracted a pneumonia which, according to his biographer, M. Boisseau, killed him because he refused to be bled, believing that his malady was one of depleted vitality, which did not require that treatment. This same biographer speaks of him thus: "He was an experimental physiologist of the highest order, characterized especially by the inventiveness and skill with which his experiments were carried out, and by his conservatism in drawing conclusions." Flourens says of him: "Legallois, who knew neither the prestige of eloquence, nor the easy success which arises through the influence of friends, modest precurser of the modern science of the nervous system, died at his post, not having obtained the renown which should, in justice, have been his."

The experiments of Legallois which bear upon the question of the cause of the heart-beat, and with which, therefore, we are concerned at this time, appeared in the year 1812 in a publication entitled: "Experiments on the principle of life and particularly on the principle of the motion of the heart, and on the seat of this principle." An American translation appeared the following year in Philadelphia. Legallois' experiment was a simple one. He crushed the spinal cord of a rabbit suddenly, and observed that the heart stopped beating. His conclusion from this experiment was that whatever might be the case in the frog, in the rabbit the heart is dependent, for its power to contract, upon the spinal cord. In other words, he concluded that the origin of the beat of the mammalian heart is neurogenic.

In the year 1810, Sir Benjamin Brodie delivered the Croonian lecture before the Royal Society. His subject was: "On the influence of the Brain on the action of the Heart, and the generation of Animal Heat." This was two years before the appearance of Legallois' paper, and while there is no reason to suppose that Brodie knew anything about the work of the French investigator, it is certainly an interesting coincidence that these workers should have hit upon such similar lines so nearly at the same time. It is equally interesting that they reached conclusions diametrically opposed to each other. The work of Brodie, to be sure, had to do with the brain, and that of Legallois with the cord. Brodie reported that he could cut the head off a dog or rabbit and if artificial respiration were established promptly, the heart would keep on beating normally. He concluded that the beat of the mammalian heart is independent of the brain, whatever may be its dependence upon lower nervous centers.

Benjamin Collins Brodie was born at Winterslow in Wiltshire in the year 1783. His father was a clergyman of the established church. At the age of eighteen he went up to London to begin the study of medicine. In the early part of 1803 he came under the tutelage of the distinguished British physiologist, Sir Everard Home. It was to the influence of this scientist, undoubtedly, that we must attribute the turning of the young physician to scientific pursuits. It appears that his reputation as a physician and scientist rose rapidly, for seven years after his first connection with Sir Everard Home he was invited to deliver the Croonian lecture. This lecture is his first published contribution to physiology. He was elected a Fellow of the Royal Society the same year, and the next year, 1811, was awarded the Copley medal, being at this time twenty-eight years old. For certain surgical services performed upon the person of George IV. and his successor, William IV., he was knighted by the latter monarch soon after his accession to the throne of England. He died at his seat, Broome Park, Surrey, at the age of eighty.

Whether or no the work of Brodie was influenced by that of Legallois, the two British scientists who were the next to take up the study of the heart-beat were, according to their own statement, led to do so on account of the conclusion of the French scientist that the beat depends upon the spinal cord. In the year 1815 two papers were read before the Royal Society by Dr. Wilson Philip,[2] both of which dealt with the relation of the nervous system to the action of the heart. Philip showed, first, that the spinal cord of a rabbit could be totally destroyed, without affecting seriously the beat of the heart, provided artificial respiration were maintained. He also studied the effects of various stimulations of the cord on the heart. He found that the application of alcohol to the upper part of the cord, in frogs or rabbits, had the effect of quickening the beat, while watery solutions of opium or tobacco had the opposite effect. He observed that considerable pressure could be applied to the brain or cord without affecting the heart. His conclusions from his results were that the heart is independent of the central nervous system so far as normal activity is concerned, but at the same time is subject to its influence to a considerable degree.

Wilson Philip was for many years an active worker in the fields of physiology and pathology. He was born in Scotland about the year 1770. Of his parentage or birth-place nothing is known. His medical training was obtained in Edinburgh. He was a Fellow of the Royal College of Physicians both in Edinburgh and London, and also of the Royal Society of London. He was a successful practitioner, and accumulated a large fortune, but unwise investments swept it all away, and, in 1842, he was obliged to depart hurriedly from London to avoid being arrested for debt. He went to Boulogne and from there all trace of him is lost. His scientific work was considered of great importance in his day. He was one of the first to employ the microscope in the study of inflammation. His contemporaries speak of him with great regard because of his humane and rational methods of experimenting on living animals.

The other investigator whose interest was aroused by the work of Legallois was William Clift,[3] whose paper was also

[2] Philip, Proc. of the Royal Soc. London, 1815.
[3] Clift, *Ibid.*, 1815.

read before the Royal Society in 1815. This worker studied the effect of destroying the spinal cord in fishes. The particular species examined by him was the carp. He found that destruction of the cord by means of a fine red-hot rod had the effect of quickening the beat for three or four contractions, but after that was without influence on the heart. He pointed out that Legallois' result was due to the suddenness and violence of his operation. He made the incidental observation that the heart of the carp comes to rest when exposed to the water (presumably fresh) in which the fish is swimming, quicker than when exposed to air.

The life of this man, William Clift, is a very interesting one. He was born in a small town in Cornwall in 1775. His mother was left a widow while he was a small child, and his early years were spent in deep poverty. He was, however, able to attend school in the neighboring town of Bodmin. Here his taste for drawing came under the notice of Mrs. Gilbert, the wife of a local gentleman, and sister-in-law of the distinguished anatomist, John Hunter. This lady recommended Clift as an apprentice to Hunter on account of his quickness and his natural taste for drawing which, she said, was shown by his eagerness "to come into her kitchen in Cornwall, and make drawings with chalk on the floor." Arrangements for his apprenticeship to the anatomist were completed, and, in 1792, Clift came up to London to enter upon his service, his duties were to write at Hunter's dictation, to make drawings, to dissect, and to take part in the care of the museum which Hunter was establishing in the back part of his house. He was with Hunter only a year, when the connection was severed by the death of the latter. During this year the young apprentice conceived a strong affection for his master, and was always active in refuting the calumnies with which Hunter's envious rivals sought to detract from his reputation. Clift was employed for the next six years by Hunter's executors to care for the collections which his late master had spent years in accumulating. For this service he received the sum of seven shillings a week, and upon this amount he lived notwithstanding the fact that food was at war prices. During these six years Clift devoted himself to the care of the collections, with such success that when, at the end of this time, they were purchased by Parliament, they were in much better condition than at the death of Hunter.

In 1800, Parliament turned the collections over to the Corporation of Surgeons, a body which became afterward the Royal College of Surgeons. Clift was retained as conservator of the museum at one hundred pounds a year, and continued in this position for fifty years, retiring, ultimately, on his full salary of four hundred pounds a year. During his tenure of the curatorship he busied himself with researches in comparative anatomy and physiology, many of which were of considerable importance. He was a man of most lovable disposition, and was held in the greatest esteem by his scientific contemporaries. Through the influence of Sir Humphry Davy he was elected a Fellow of the Royal Society in 1823. Cuvier, Sir Charles Lyell, Sir Benjamin Brodie, and other scientific men acknowledge their indebtedness to him for information and help in completing their researches. He died in London in the year 1849.

After the appearance of these three papers which have been just spoken of, no further contributions on this subject were made to the Royal Society for thirty years, and with the exception of an isolated observation occasionally, no more work seems to have been done on the heart-beat in England for that length of time. About the year 1836, Todd's Encyclopedia of Anatomy and Physiology was published in England. This work was an attempt to give a complete résumé of the anatomical and physiological knowledge of that time. The chapter on the heart was contributed by John Reid, an anatomist of Edinburgh. In common with the other anatomists of his day, Reid delivered lectures and performed researches in physiology as well as in his own more particular subject. He begins the part of his article that is devoted to the causation of the heart-beat, by a review of the teaching of Haller on the subject. It will be remembered that Haller believed the irritability of the heart to be an intrinsic property of the muscle substance, and that this property is normally called into action by the stimulating influence of the blood upon the tissue. With regard to the question as to whether or not the heart requires the influence of the blood or any other stimulus to call it into action, Reid quotes an experiment,[4] apparently his own, in which the heart of a frog was placed under the receiver of an air-pump and the air exhausted from around it. The beat continued undisturbed under these conditions, although the possible stimulating action of the air was excluded. He does not accept this, however, as conclusive evidence that the heart is able to beat without direct stimulation, because, as he says, the mere contact of the organ with the surface upon which it is lying may be sufficient stimulus for a structure having such excessive irritability as the heart may be supposed to possess. In connection with his discussion of the influence of the blood on the heart-beat, a curious notion crops out, which seems to have been quite prevalent about that time. I have come upon the same notion in the writings of others of that period. The idea seems to have been that the chief function of the heart was to pump itself free of the blood that continually flowed into it. I quote Reid's own words on the subject. "When the blood is forced on more rapidly toward the heart, as in exercise, its contractions become proportionally more frequent. If the contractions of the heart were not dependent upon the blood, and their number regulated by the quantity flowing into its cavities very serious and inevitably fatal disturbances in the circulation would soon take place." Having concluded that heart muscle, like skeletal muscle, is directly dependent for every contraction upon some form of external stimulation, he passes to the question as to where the irritability of the heart resides. Is it a property of the muscle substance, or is it mediated only through the nerves of the organ? He quotes the experiments of Wilson Philip, Clift, and others which show that the heart is independent, at any rate, of the brain or cord. As will be brought out presently, those who still maintained the neurogenic origin of the heart-beat attributed it to sympathetic nerve centers outside the cord. Brachet,[5] a French observer whose work appeared in 1834 believed that it resided in the cardiac plexus, because he found that extirpation of this structure resulted in the immediate and permanent arrest of the heart. Reid

[4] Reid, Todd's Encyclo., Vol. II, p. 611, 1836-39.

[5] Brachet, Rech. exp. sur les fonct. du syst. nerv. ganglion. Paris, 1830, p. 163.

questions the conclusiveness of Brachet's experiment on the ground that so much time was required for the operation, and so much injury to heart tissue was involved in it, that it would be a matter of surprise to find the heart beating at its end. While he admits that there is abundant evidence for the fact that the heart is influenced to a greater or less extent by the central nervous system, Reid nevertheless concludes that the sum-total of knowledge indicates that the heart muscle possesses in itself the property of responding to stimulation by contraction.

The facts that I have thus far recorded, show clearly, I think, that among English physiologists there was very little inclination to depart from the views originally expressed by Haller, so far, at least, as they looked upon the irritability of the heart as a property of its muscular substance. What little insight we have had into the French standpoint has indicated that among the workers of this land the neurogenic theory was looked upon with favor, to say the least. I wish now to give some account of the views which were being developed in Germany during this same time. I am indebted to the article in Wagner's Handwörterbuch der Physiologie, Vol. II, by G. Kuerschner,[6] on this subject, for most of the facts which I am able to present concerning the German point of view, up to his time, 1844. Unfortunately I am unable to give any account of this man's life, nor to form any estimate of his fitness for the task of presenting the theories of his time regarding the topic in hand. The fact that he was selected to discuss the subject of the heart's activity in so important a work as Wagner's Handwörterbuch would seem to be sufficient guaranty of his fitness for the task, but the curious theory he proposes in explanation of the heart-beat would lead one to doubt his possession of conservative judgment. No one is mentioned in the Cyclopedie der Aertzte, nor in the large German national encyclopedia of biography with whom I could certainly identify him. His references are by no means so complete as might be desired, hence I shall be obliged to refer to much of the work done in Germany in general terms.

The German method of attacking the problem, according to Kuerschner, was to make careful comparative studies of the heart, both with skeletal and plain muscle, and then draw conclusions by reasoning from analogy. The histological and chemical studies of the heart that were made during the early years of the nineteenth century, indicated a close resemblance between the structure of the heart and of skeletal muscle. The question as to whether the heart muscle could be made to respond to stimulation in the way in which skeletal muscle does, was for a long time the subject of much controversy. The discussion included both the question as to whether or not the heart could be directly stimulated, and the problem of its responsiveness to stimulation through its nerves. Volta, Valli, Klein, Pfaff, Behrends, and Bichat decided that direct galvanic stimulation of the heart's substance was without effect upon it so far as arousing activity was concerned. Humboldt,[7] Fowler,[8] and Nysten, on the other hand, were able to prove conclusively that under proper conditions the heart could be excited to definite motor response by galvanic stimulation. The Italian physiologist, Fontana, observed that in spite of strong mechanical stimulation, such as pricking with a sharp instrument, the diastole of the heart proceeded to its end. He interpreted this to mean that the heart does not respond to this sort of stimulus. Other observers, however, were able to show that if the mechanical stimulus is properly applied, response can be obtained also to this kind of stimulation. Equally discordant results were obtained in the attempt to determine whether the heart can be stimulated through its nerves. Humboldt reported that he was able to excite a heart to contract by galvanic stimulation of the nervi cardiaci. Burdach[9] found that either chemical or mechanical stimulation of the cervical sympathetic in dying rabbits, strengthened the contractions of the heart. Neither Kuerschner nor Joh. Mueller could obtain the result reported by Burdach, although Kuerschner reports a single instance in which each stimulation of the common vago-sympathetic trunk in a dying dog was followed by a single contraction. Valentin[10] and Volkmann observed variations in the heart-beat after stimulation of the spinal accessory nerve within the cranial cavity. In spite of these variant results the conviction fastened itself upon the minds of practically all the workers in this field, that the heart, like skeletal muscle, can be stimulated either directly or through its nerves. The great similarity of the heart to skeletal muscle in so far as ordinary response to stimulation is concerned, having become generally admitted, the next problem to be faced was the comparison of the rhythmicity of the heart with that of structures in which ordinary skeletal muscles are involved. To those who were looking for analogies between the action of the heart and that of organs whose activity is admittedly of nervous origin, this study very soon developed facts which seemed to offer conclusive proof of the neurogenic origin of the heart's activity. The most important of these was the observation that as a heart is gradually dying, its rhythmic property disappears before the power of the individual fibers to respond to stimulation is lost. It was also shown by Kuerschner that if a heart be cooled down with ice-water, any of its chambers can be provoked to response by proper stimulation without the contraction spreading so as to involve other chambers than the one stimulated. Strictly analogous phenomena in other rhythmic structures, structures whose activity is evidently nervous, are quoted by Kuerschner. He says, for instance, that if the brain of an animal be destroyed, the contractions of the œsophageal muscles in swallowing are orderly and normal at first, but subsequently this sequence disappears and then stimulation of any muscle is followed only by contraction of that muscle, and not by the entire act of swallowing as at

[6] Kuerschner, Wagner's Handwörterbuch d. Physiol., 1844, Vol. II, p. 70 et seq.

[7] Humboldt, Gereizte muskel- und nervenf., Vol. I, p. 312, 1797.

[8] Fowler, Exper. on Animal Electricity. London, 1794.

[9] Burdach, Physiol., Vol. IV, p. 464.

[10] Valentin, De funct. nervorum cerebral et symp. Berne, 1839.

first. He cites as another example of the same sort, that if the head of a lizard be severed from its body just behind the occipital foramen, the respiratory movements of the head and neck continue normal for a time, but ultimately local stimulation meets only local response, as in the case previously cited. I shall give you Kuerschner's reasoning from these facts in his own words:

"These experiments teach that, in general, rhythmic activity is dependent upon the central nervous system, and not upon the muscles. It is well known that the central nervous system loses its irritability as the result of decapitation or poisoning much quicker than do the muscles. In this the heart is analogous. It loses its rhythmic property before the power of the individual muscles to respond to stimulation is lost. The conclusion can scarcely be avoided that in the heart the combination of contractions of the different parts results, not from the irritability of their muscle masses, but from the combination of these muscle masses, by means of nerves, with a central organ of the nervous system. Hence all hypotheses for the explanation of the heart's rhythm which go back to the independent irritability of the heart tissue are excluded. Among them must be placed the opinions of Haller."

The argument, which I have just given appeared to the German physiologists perfectly sound and conclusive. The question as to what central nervous organ is to be looked upon as the source of the heart's rhythmic action promised, however, to present some difficulty. The experiments of Brodie, Philip, Clift, and others had showed beyond doubt that neither the brain nor the spinal cord is essential to the rhythm of the heart. Magendie had removed all the sympathetic ganglia of the neck, along with the first dorsal ganglion, without disturbing the heart's action. There was also to be considered the fact of the long-continued beat of the isolated cold-blooded heart. To meet all these difficulties, Joh. Mueller advanced the idea of intra-cardiac ganglia. Fortunately for his suggestion, the existence of ganglion cells in the heart was shortly demonstrated by Remak,[11] Volkmann, Bidder, and by Mueller himself. To add to the assurance which this discovery gave, it was shown that these nerve cells are most abundant in those parts of the heart in which its rhythm originates, and in which experiment shows it to be most irritable, namely, the venous portion. Investigators were unable to prove experimentally that the rhythm of the heart depends upon the intra-cardiac ganglion cells, but they made a great deal of a clinical case reported by Dr. J. Heine,[12] son of the distinguished orthopedic surgeon of that name, from one of the Vienna hospitals, in the year 1841. The case was of a man whose "*nervus cardiacus magnus*" was bound up into a black knot the size of a hazel-nut just beneath the arch of the aorta. The nerve was somewhat thickened where it entered into the knot. This man suffered from periodical intermittence of the heart-beat. The interpretation of this case was as follows: The heart must be under the influence of the nervous system, or this malformation of the cardiac nerve would have had no effect. On the other hand, the seat of the heart's dependence must be lower down than the level of this disturbance or, instead of presenting the phenomenon of periodical intermittence, the heart would have stopped beating altogether.

A satisfactory nervous mechanism for carrying on the heart-beat had now been supplied. It remained to suggest, and if possible prove, the way in which this mechanism acts to bring about the rhythmic beat of the heart. Joh. Mueller[13] proposed an ingenious hypothesis which involved a conception of the mode of action of the sympathetic ganglion cells that has persisted in physiology to a greater or less degree even up to the present. He was led to his idea by the observation that when the cœliac ganglion is stimulated with potassium hydrate or some similar agent, in a rabbit with exposed viscera, there is a long latent period between the application of the stimulus and the response of the intestines.[14] He concluded that the sympathetic ganglion cells bear the same relation to the nerve impulse that the leyden jar does to the electric spark. In other words, the ganglion cell requires to be charged, an operation which consumes a certain amount of time. Based upon this assumption, Mueller's explanation of the rhythmic action of the heart was as follows: A steady stream of impulses is to be conceived as flowing into the heart from the central nervous system. These impulses, instead of arousing the heart, accumulate in the ganglion cells until they reach a certain maximum, when they are discharged all at once, producing their effect upon the heart. By assuming this property for the cells of the sympathetic ganglia, the rhythmic nature of the heart-beat is satisfactorily explained. Kuerschner takes exception to Mueller's hypothesis on two grounds, in the first place he says that the assumption of a peculiar property for the sympathetic cells, different from that possessed by precisely similar cells in the cord, is entirely unwarranted. Moreover, he argues, the beat of the heart like the action of every other bodily organ, should be looked on as purposeful, adjusting itself to the varying requirements of its function. According to the hypothesis of Mueller, the action of the heart is regulated entirely from the outside, and no mechanism is suggested by which the necessary adaptations can be made. In all the other rhythmic structures of the body, the respiratory apparatus, the œsophagus, the intestines, etc., a means of suiting the activity of the structure to the work it has to do exists. Why then may we not look for a similar regulatory device in the heart?

In proposing a hypothesis on his own account, Kuerschner sets out to fulfil the following conditions. He must provide a way by which rhythmic nervous stimuli can fall into the heart from the ganglion cells imbedded in its own substance. These rhythmic nerve impulses must be adapted so that they can vary with the varying needs of the body, and they must also be under the influence of the external stimuli which are

[11] Remak, Mueller's Archiv, 1844, p. 463.
[12] Heine, Mueller's Archiv, 1841, p. 234.
[13] Joh. Mueller, Physiologie, 1843, Vol. I, p. 630 et seq.
[14] Joh. Mueller, Physiologie, Vol. I, p. 631.

continually falling upon the heart from the blood flowing through it. He lays great stress upon the idea that the most satisfactory way in which a purposeful adjustment of the heart's action can be imagined, is by the supposition that every response of the organ comes as the result of a definite stimulus which reaches it from the outside, usually through the blood. All experiments indicate that the heart beats only in response to stimuli. In the cases in which excised hearts continue active for a long time, the air can be looked upon as the efficient stimulus. Even the experiment of Reid, in which a heart continued to beat in an exhausted chamber, is an illustration of the same principle, for when one considers the great pressure of the ordinary atmosphere, he could not expect otherwise than that the withdrawal of so great a load should act as a most efficient stimulus. It is evident that the simplest, if not the only way, by which stimuli applied to the surface of the heart can bring about the discharge of nerve cells, is through a reflex mechanism. Kuerschner proposes, then, to see if a reflex arc can be logically established within the heart, and if so, to inquire whether a rhythmic source of sensory stimulation can be demonstrated. "No one can doubt," says Kuerschner, "the existence of sensory nerves in the heart. The pains which arise in diseases of that organ are proof enough." He finds also another proof of their presence in the fact noted by Haller, that the inner surface of the heart is more sensitive than the outer one. Moreover, Henry [15] and afterwards Joh. Mueller,[16] found that opium and nux vomica were without effect on the outer surface of the heart, but promptly arrested its beat when applied to the inner surface. The conclusions to be drawn from these results are: 1st, that the action of the stimulus in the one case, and of the drug in the other, was upon sensory nerves; 2d, that these nerves are more abundant on the inner than on the outer surface of the heart. It is scarcely to be supposed that if the action were simply upon muscle substance one surface would be found to differ in response from the other one. If it be admitted that sensory nerves are present in the heart, some normal function for them is to be sought, for it is scarcely to be supposed that sensory nerves are present for no other purpose than to give warning of disease. The simplest explanation of their function that can be offered is to suppose that they form the sensory side of a reflex mechanism. The fact that the response of the heart to stimulation is always orderly, no matter to what part of its surface the stimulation is applied, is another argument for the idea that stimulation affects sensory nerves. The stimulus may be applied at the tip of the ventricle, but if the heart is in good condition the response always begins at the auricle and sweeps over the heart in the usual way. Only two other explanations for this fact are possible. Unless the stimulus at the tip of the ventricle affects a sensory nerve, the impulse must be transmitted through the muscle substance itself to the auricle, or else motor nerves on their way to the venous part of the heart must curve around so as to pass by the tip of the ventricle. Moreover, since stimulation at any point on its surface results the same as at the tip of the ventricle, it would have to be supposed that motor nerves lead from every part of the heart to the auricle. By far the most sensible view, in Kuerschner's opinion, is to admit the presence of sensory nerves. Having demonstrated to his own satisfaction a reflex arc, Kuerschner now proceeds to seek for a normal rhythmic source of sensory stimulation, by which his reflex mechanism may be operated. It is evident at once, that this source of stimulation is to be found in the blood. Not only must this be the case in order that the heart may fulfil its function as a purposeful mechanism, but no other possible source of stimulation presents itself. There are two alternatives as to the way in which the stimulating action of the blood may be exerted. It may stimulate chemically or mechanically. Four considerations are presented by which, according to Kuerschner, chemical stimulation is excluded: 1st, if the stimulus of the blood were chemical, a single drop should be as effective in arousing a response as a large quantity, hence the heart, under these conditions, would never have a chance to become filled with blood, but as soon as the first drops entered it the next contraction would ensue; 2d, it is a general law of the body that wherever chemical stimuli are in play, not serous but mucous membranes are present, whereas in the heart, as is well known, serous membranes are the only ones that exist; 3d, a fluid which feeds the heart, cannot well act at the same time as a chemical stimulus to it; 4th, if the stimulus is chemical, the two sides of the heart must have entirely different sorts of irritability since they react alike, while one side contains only arterial blood, and the other only venous blood, a fluid differing from arterial blood so far as its chemical nature is concerned, to a very marked degree. This last great difficulty in explaining the similar action of the two sides of the heart, is entirely obviated by the assumption that the stimulating action of the blood is mechanical, for arterial and venous blood are perfectly similar so far as physical characteristics are concerned, and so would have, as a matter of course, equivalent mechanical effects. Another, and quite distinct, set of phenomena also argue strongly in favor of the view that the influence of the blood upon the heart is mechanical. These are the phenomena connected with the rise of cardiac sensations into consciousness. Such sensations appear to us always as pressures. The pains which result from diseases of the organ are pains of too severe pressure. The heart sensations which we have as the result of violent emotions are sensations of pressure. Trouble, grief, and care press upon the heart. Observations show that often acute inflammations of the heart substance are felt only as pressure in the heart region. Kuerschner now proceeds to show how the mechanical stimulus works and begins by enunciating what is to him the vital point of the whole proposition. This point is as follows: "It is not to be assumed simply that the stimulus for contraction is aroused when the heart is full of blood, but *when it can be filled no further.* The contraction is thus aroused at the instant most suited to the needs of the circulation." When he begins to develop this

[15] Henry, Edinburgh Med. and Surg. Jour., 1832.
[16] Joh. Mueller, Physiologie, Bd. I, p. 636, 1840.

idea, which he does by attempting to apply it to conditions under which the heart-rate varies, he involves himself at once in a maze of difficult and complicated argument. I will not weary you further with the pointless, and well-nigh endless mass of logic with which he attempts to establish his proposition. I wish to say, however, that in his argument the same idea appears as in the discussion of the same topic by John Reid, and of which I spoke in that connection. I refer to the idea that the purpose of the heart-beat is chiefly to unload the heart from the weight of blood which is constantly flowing into it. This theory of Kuerschner's was published in 1844. It seems to have attracted almost no attention, a fact which is to be explained, in all probability, by the circumstance that at about this time began a great flood of discoveries which, although not overthrowing the neurogenic theory, put an entirely new face on the whole problem.

In 1845 the brothers Eduard and Ernst Heinrich Weber discovered the inhibitory character of the vagus nerve, in its action upon the heart. This discovery ranks, undoubtedly, among the most important physiological contributions of the nineteenth century. In view of its great significance, a quotation from the authors' own account of their experiments may be of interest. Their paper appeared in the third volume of Wagner's Handwörterbuch,[17] the second part. I have found it convenient to paraphrase and abridge considerably their description. They report six series of experiments. In the first set they beheaded a frog and then stimulated the cord, having one electrode at the upper end and one at the lower. This procedure had no effect upon the action of the heart; nor did they obtain any when both electrodes were placed upon the cut upper end of the cord. When, however, in an unbeheaded frog they placed one electrode in a nostril and the other on the cut surface of the cord at the level of the fourth or fifth vertebra, stimulation was followed, after one or two pulsations, by complete standstill of the heart. When the stimulus was removed, the heart began, after a few seconds, to beat again; slowly and feebly at first, but after a short interval with the original rate and force. The standstill was in diastole, and the heart remained full of blood.

The second set of experiments were for the purpose of determining from what part of the nervous system this inhibitory influence proceeded. The head of a frog was separated from the vertebral column in such a manner that the heart, the lungs, and the abdominal viscera retained their normal connections with the head. The electrodes were placed close together on the cut upper surface of the medulla. Stimulation was followed by stand-still of the heart, sometimes completely, sometimes only partially, according as the animal was fresh and vigorous or not, according to the degree of exhaustion of the nervous parts, and according to whether the stimulating current were employed to advantage or not. The heart remained at rest under continued stimulation until the vagus nerve became fatigued, when, in spite of the stimulus, the heart resumed its normal activity. These effects arose entirely from stimulation of the brain, inasmuch as removal of the spinal cord did not, as we have just seen, produce any change in them.

To make a more exact determination as to what part of the brain these effects came from, the electrodes were placed very close together, and the brain of a frog, from which the roof of the skull had been entirely removed, was carefully explored. It was found that stimulation of the cerebral hemispheres has no effect upon the heart. When the corpora quadrigemina were stimulated, the heart came to rest after three contractions. To prove whether this result arose from the corpora quadrigemina themselves, or was due to spread of current to the medulla, a cut was made with great care between these two portions of the brain, leaving them, however, in contact. Stimulation of the corpora after this operation had not the slightest effect upon the heart. This experiment made it evident that this power to arrest the heart is present in the corpora quadrigemina. In order to determine the lower limit in the brain of this inhibitory function, a series of exploratory stimulations were made, beginning at the brachial plexus, and working up the cord. No heart effects were obtained from these stimuli until the level of the lower end of the calamus scriptorius was reached in the medulla. At this point stimulation caused standstill. The medulla was then sectioned at this point, and stimuli were applied first to the upper cut surface, and then to the lower. Stimulation of the upper surface caused standstill, but no effect was seen when the lower surface was tested. By this means they mapped out the area of the brain from which inhibitory fibers arise as extending from the corpora quadrigemina to the lower end of the calamus scriptorius in the medulla.

The next question was through what nerves the inhibitory influences are conveyed. One vagus in a frog was cut and stimulated peripherally without effect on the heart, but when both vagi were cut, and both stimulated at the same instant, the arrest ensued. Their conclusion was that this property of inhibition requires the combined influence of both these nerves for its successful accomplishment.

The sympathetics were studied to see whether they shared the function of the vagi in this regard. It was shown that they do not convey inhibitory impulses to the heart.

To ensure that the vagus effects were not due to escape of stimulus to the heart over these nerves, a device was prepared by which any current that might pass down either vagus, would be short circuited before it reached the heart. The effect of stimulation after this device was used was exactly the same as before.

This experiment completed the chain of evidence, so far as the frog's heart is concerned. It only remained to see whether the same mechanism exists in the warm-blooded animals. The Webers tried this upon a kitten four weeks old by exposing and stimulating the vagi in the neck. They found that the heart was arrested in the kitten, just as in the frog, and also that it would break through long-continued stimulation in precisely the same way.

[17] Weber, Ed., Wagner's Handwörterb. d. Physiol., Vol. III$_2$, 1846, p. 43 et seq.

The Weber brothers were led by their experiments, to draw the following conclusions as to the source of the rhythmic action of the heart. The sympathetic nerves were to be considered as the motor nerves of the heart. These act by innervating the intra-cardiac ganglia. These ganglia, however, must possess the power of independent rhythmicity to a large degree, since the isolated heart is able to beat. The vagus fibers are inhibitory, and their inhibitory power is exercised in the heart in exactly the same way as in other structures that are under nervous control. That is to say, they act by inhibiting the ganglia from which the normal impulses of the heart arise. When we recall the fact that the idea of the inhibition of nerve centers by means of nerve impulses was a familiar one at that day, whereas such a thing as direct inhibition of muscles through nerves had never been thought of, the conclusion of the Webers is seen to be the most natural one they could have drawn.

In 1850 Schiff[18] discovered the existence of the refractory period. His discovery was corroborated, and a careful study of the phenomenon made, by Kronecker and by Marey the following year. This discovery was helpful to those engaged in the attempt to explain the heart-beat, because it removed the necessity of providing a source of rhythmic stimulation. Since the heart is refractory during a part of its beat, all that is necessary in order to explain its rhythmic action is to demonstrate the existence of a source of constant stimulation. Its own property suffices to convert this constant stimulus into rhythmic response. To the "motor ganglia" in the heart substance was assigned this role, and this idea was regularly incorporated into the neurogenic theory.

In the early fifties the celebrated experiments of Stannius[19] were performed. This observer placed a ligature exactly at the junction of the sinus with the auricle and the part of the heart beyond the ligature stopped beating. He then tied a second ligature in the auriculo-ventricular groove and the beat of the ventricle was resumed. The explanation of the stoppage which followed the first ligation, was simply that the source of the nervous discharges upon which the heart depended for its action, Remak's ganglion in the sinus, had been cut off. To explain the revival of activity in the ventricle as the result of placing a ligature in the auriculo-ventricular groove, recourse was had to the fact that Bidder's large ganglion lies in this groove in such a position that ligation might stimulate it. To this ganglion was assigned a subsidiary emergency role. Although supposed to be normally inactive so far as influencing the heart's rhythmic beat was concerned, it was supposed, under this special stimulus, to become active and efficient as a means of arousing the ventricle to contract rhythmically.

At the conclusion of the statement of the early work in England, mention was made of the fact that among British physiologists the myogenic theory of the heart's action remained generally in favor. Beginning about this time, 1850, a great many facts began to be brought out which strengthened the British position very much, and, as a matter of fact, put the believers in the neurogenic theory rather on the defensive. The experiments of Bernstein,[20] published in 1876, were especially welcome to them, because they formed the first important contribution to the neurogenic side of the argument during the period of twenty years succeeding the work of Stannius, a period which had been very productive of evidence on the other side. Bernstein showed that if a clamp were adjusted across the middle of a beating ventricle and then screwed tight, the portion of the ventricle beyond the clamp would come to rest. This portion of the heart had been shown to be free from ganglion cells, hence this experiment was interpreted as showing that parts of the heart which do not contain ganglion cells cannot beat if their connection with those parts in which nerve cells are present is cut off.

As recently as 1894 a strong argument in favor of the "motor ganglion" theory was advanced by Kaiser.[21] He based his argument upon a modification of the experiment of Stannius. It will be recalled that when a ligature was tied in the auriculo-ventricular groove of a heart which had been brought to rest by tying off the sinus, contractions were aroused again in the ventricle. Kaiser showed that if Bidder's ganglia were removed, ligation of the auriculo-ventricular ring was not followed by rhythmic contractions of the ventricle. He showed, moreover, that stimulation of the intact auriculo-ventricular ring is always followed by a series of several contractions, whereas stimulation of the same area after extirpation of Bidder's ganglia is followed by only one contraction for each stimulus, as is the rule for the heart-substance in general. The strongest opponents of the neurogenic theory were obliged to admit that Kaiser's argument, as based upon the experiments just quoted, was well-nigh incontestible, since no other reasonable explanation of his results can be given than to suppose that Bidder's ganglion has a motor influence on the heart's activity. An account of the way in which Kaiser's experiments were reconciled to the myogenic theory by its upholders, will be given in its proper place in connection with the review of the modern development of that theory. The present status of the neurogenic theory is practically that of Kaiser, since he is probably the latest to argue in its favor.

[18] Schiff, Arch. f. Physiol. Heilkunde, 1850, Vol. IX.

[19] Stannius, Arch. f. Anat., Physiol., u. wiss. Med., 1852, S. 81 et seq.

[20] Bernstein, Centralbl. f. d. med. Wissen., Berlin, 1876, S. 385.

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THE JOHNS HOPKINS HOSPITAL BULLETIN.

The Hospital Bulletin contains details of hospital and dispensary practice, abstracts of papers read, and other proceedings of the Medical Society of the Hospital, reports of lectures, and other matters of general interest in connection with the work of the Hospital. It is issued monthly.

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THE PARTIAL OCCLUSION OF BLOOD-VESSELS, ESPECIALLY OF THE ABDOMINAL AORTA.

A PRELIMINARY REPORT BY DR. HALSTED.

At the meeting of the Johns Hopkins Hospital Medical Society, on March 20, 1905, a brief preliminary report was made of the results of a large number of experiments performed in the past year by Dr. Sowers and myself upon the abdominal aorta and other large blood-vessels of dogs.

It had occurred to one of us that possibly the aorta might be successfully occluded in man if the operations were undertaken in several acts instead of one. The notion of gradual compression in the ordinary use of the term was entertained only to be definitely discarded because of the seemingly insurmountable difficulty of preserving asepsis. A sinus must form about any instrument leading from the aorta to the air, and, sooner or later, such a sinus necessarily becomes infected. The method, therefore, should, we thought, be one permitting, in each entre-act, complete closure of the wound; the apparatus or material applied to the aorta should not be bulky nor endanger, by its form or substance, the adjacent parts; and it should admit of easy readjustment at subsequent operations. Metal bands of silver and aluminum were employed with the belief that at each operation the amount of constriction could be regulated to a nicety. With the aid of a clever jeweller an instrument was devised to curl the metal strip, in situ, in perfect cylinder-form, about the vessel. The tightening of the band, the cylindrical form being preserved with great care, was completed with fingers and tweezers, but ultimately, when narrower bands were used, the tweezers could, fortunately, be discarded. The instrument for curling the band was also in the majority of cases finally dispensed with.

We attempted rather persistently but unsuccessfully to determine accurately the blood pressure in the femoral arteries during and after the application of the band; and Dr. Haller is now devising and constructing for us an instrument on the principle of the Erlanger instrument to enable one to determine the blood pressure in small and large arteries without dividing them. Calculations, therefore, as to the amount of occlusion were roughly determined by the fingers on the aorta and femorals.

For some weeks we feared that the sharp edges of the bands would cut through the pulsating and constricted aorta, and considered several methods to obviate, if necessary, this danger. On the twelfth day of the operation a dog died from hemorrhage, the result of ulceration at the upper edge of the band and we feared that the procedure might be doomed; but no further hemorrhage occurring we resumed, in a few weeks, the experiments. Then, after about 3 months, investigating in several dogs the conditions at the site of the band, we found to our chagrin, that just as we had feared, the wall of the aorta embraced by the band was, in almost every instance, atrophied, being reduced in some cases to hardly more than a film in thickness. Notwithstanding this observation the experiments went on uninterruptedly, a new series being instituted with the hope that, with an improved technique, and the employment of narrower and thinner bands, the walls of the arteries might retain their vitality, at least for a time sufficiently long to justify a second interference, and possibly the complete interruption of the blood current at a point just above the band. The width of the bands was reduced from 4 or 5 mm. to 2 or 3 mm., and the thickness from 32 and 33 degrees of fineness to beyond the highest numbers of our sheet metal scale, to what we term Nos. 37, 38, 39, and 40. On the carotids and femorals metal still thinner might perhaps be used. Bands so narrow and so very thin are easily rolled with the fingers. It is well to give the band approximately the proper curl before placing it on the artery. From the very first experiment we endeavored in each instance to roll the band as perfectly, as cylindrically, as possible, flattening of it being studiously guarded against for obvious reasons. Attempts to diminish the blood pressure very gradually and with accuracy are, of course, made futile by an imperfection in the rolling of the band. A flattening or imperfectly rolled band might, even if loosely applied, injure the intima and so cause thrombosis and completely interrupt the circulation. For these and other reasons silver wire, which was tried, was found impracticable. About ninety experiments were made on sixty-eight dogs. The technique of our operating rooms at the Johns Hopkins Hospital was observed in every particular and hence much time was consumed by the operations; but we are well repaid for the care exercised by the absence of wound infection. The buried, continuous, silver wire suture of the skin and rubber gloves for operator and assistants seem invaluable in experimental surgery when wound infection must be avoided. We are greatly indebted to Messrs. Cowles, Faris, Haller, Langford, and other fourth year students for their faithful assistance and interest and useful suggestions.

Summary.

(1) Thrombosis has not been observed in a single case. In a few of the specimens, however, proximal to the band, in the occluded artery, a little caruncle-like body, suggesting the substitution of a minute clot, has been present.

(2) Applied tightly enough to completely interrupt the circulation, the band has caused atrophy and sometimes complete absorption of the aortic wall; in such cases hemorrhage has invariably been prevented by the formation of connective tissue.

(3) With two or three exceptions there has been no evidence of adhesion of the folded intima *under the band;* aortic walls folded on themselves so snugly that, the band being

still in place, water could not be forced through with a syringe, could easily be smoothed out and the full lumen reestablished on removal of the band.

(4) Less snugly, loosely, and very loosely applied bands may remain on the aorta, femorals and carotids for months without causing macroscopic injury to the walls of the artery. In experiments of this variety the band after, say, one hundred days, shimmers brightly under a normal looking peritoneum, causing no visible reaction, and it may be as easily removed from the aortic wall as when originally applied. The probe point of a fine scissors passed into the lumen of the aorta and thus on through the band, dividing it and the aortic wall, reveals a perfectly normal looking intima and an aortic wall which, on gross section, evidences no change in texture and usually none in color.

We are encouraged to believe that there may be a place in surgery for the partially occluding band. Recently we have twice had occasion to use it on the human subject.

CASE I. *To the left common carotid was applied an aluminum band which almost occluded it.*—Even in this case slight head symptoms persisted for several months making it seem likely that complete occlusion would have been followed by severe symptoms if not by death. We regretted that, in this case, the band was inadvertently rolled tighter than intended; it could, of course, have easily been removed and reapplied but our notions being rather vague as to the precise amount of constriction which we desired and being unable to determine accurately the blood pressure distal to the band we decided to let it remain and note the results.

CASE II. *A woman asphyxiated to unconsciousness by an aneurism of the arch of the aorta.*—She was restored to consciousness and temporary relief afforded by a tube passed into the right bronchus. The skiograph seeming to indicate that the aneurism was chiefly on the left side of the sternum and the condition of the patient being so desperate I decided, having watched her for nearly half a day, that she would live only a few hours unless surgery could assist her. We exposed carefully and freely, without opening either pleural cavity, the heart, the arch of the aorta and the large vessels at the root of the neck hoping possibly to be able to encircle the aortic arch with a band of metal between the origins of the innominate and left carotid arteries; but the aneurism involved the entire arch and thus defeated our very earnest efforts to carry out the plan. The patient succumbed on the operating table before we had entirely despaired of being able to do something for her relief, and while we were still endeavoring to make a path for the band.

The smaller arteries, the ligation of which endangers merely the life of the limb may prove as suitable for partial occlusion as the aorta (abdominal and thoracic) which has never been successfully ligated in man. Meagre as our knowledge of this subject is I should probably feel it my duty to test the value of partial rather than resort to complete occlusion of the aorta, common cartoid, popliteal and other arteries whose ligation is attended with great danger to life or limb.

The partial occlusion of arteries discloses a suggestive and, I believe, a promising field for investigation in physiology and experimental pathology.

The history of the subject will be considered in a subsequent article. Of particular interest to us is the discovery that Luigi Porta, about 1846, attempted partial occlusion of arteries by means of strips of diachylon plaster applied in a way similar to that described by Brewer, who so ingeniously and cleverly closes wounds of arteries by strapping them with an absorbable plaster.

NOTES ON NEW BOOKS.

Lectures on Diseases of the Nervous System. Second Series. *Subjective Sensations of Light and Sound, Abiotrophy, and Other Lectures.* By SIR WILLIAM R. GOWERS, M. D., F. R. C. P., F. R. S., pp. 150. (*Philadelphia: P. Blakiston's Son & Co., 1904.*)

This neat but inexpensive volume contains a collection of ten lectures, all of which have been published separately before, some as long ago as ten years. Nevertheless, their appearance in book form is undoubtedly opportune, for those who are already acquainted with them will surely find time to read them again, and for those to whom they are still new not only profit but also much enjoyment can safely be promised. If it were necessary to condense this review into six lines we might well content ourselves with Dr. Gowers' own, perhaps too modest, words: "The facts I have given you are commonplace. Many of them may have been known to some of you, some of them may have been known to many of you; but one fact I am sure is true of all my hearers—for it is as true of myself as of anyone—the commonplace is, of all knowledge, that which we can least afford to despise or disregard." The first lecture on "Subjective Visual Sensations" has been re-written and several points of interest have been added. The second lecture deals with subjective sensations of sound, tinnitus aurium in its various manifestations being discussed. In the third and fourth lectures—which treat of abiotrophy or diseases due to defect of life—the various forms of atrophy are dealt with. In the essay on metallic poisoning—with lead and arsenic—the discussion of the lead-line and the various manifestations of arsenical pigmentation makes very interesting reading, but not less so the digression on the use of the term neurasthenia, which contains suggestions that every medical practitioner must ever keep in mind.

The other subjects dealt with are: Syphilis of the nervous system, inevitable failure, a study of syphilitic arterial disease, syringal hemorrhage, myasthenia and ophthalmoplegia and the use of drugs. That "the last, although given some years ago, seems to need no change in consequence of fresh knowledge" is undoubtedly true, but some amplification of the subject would certainly have been acceptable. The book is full of facts and of observations that are very helpful and suggestive, and should find a place in every medical library.

The Intestinal Catarrhs. Second edition. By EDWARD BLAKE, M. D., F. R. C. S. (*Chicago: W. T. Keener & Co., 90 Wabash Avenue, 1905.*)

This work has been published in response to a complaint from many sources that there is no English treatise on the intestinal catarrhs. It is apparently a clinical study of colitis, appendicitis, and their allies, with a section on sprue. The first chapters are concerned principally with the definition and the variety of names which are given to the condition which we usually term mucous colitis. The writer quotes seventy-six synonyms as applied to the

general catarrh of the intestinal tract. As, however, among the titles under which the author states that general catarrh of the intestines is "vaguely recognized" we find rickets, tabes mesenterica, Graves' disease, gout, rheumatic gout, dilated stomach, urticaria, psilosis, Cochin-China diarrhœa, not to speak of chordapsus, phantom tumor and senile enuresis, we must confess to being slightly puzzled.

Dr. Blake would assign the beginnings of colitis to a very early stage of existence. The occurrence of mucin and albumen during the first week of life is the first suggestion of the possibility of colitis. In an examination of the book we suddenly find a discussion of albuminuria in early life and then the report of a case of pyelitis from colitoxin. The special importance of this we rather fail to see, as also the report of a case of cystitis due to bacteriuria. Then follows a section on certain of the organisms found in the intestines. Again abruptly after this we are given a discussion of the causation of pancreatitis, cholecystitis and gall-stones. With this is an explanation of the secretion of the pancreatic juice. The startling statement is made that colitis is essentially an affection of the skin, by which the author apparently means that conditions in the skin are essentially associated with the colon. But in almost the next paragraph it is stated that gout apparently is the essential causative factor in colitis, and then a few lines further on that lack of ability to digest starch is the most important causative factor. A little later on we are suddenly thrown into a discussion as to the causes of infantile diarrhœa.

Then follows a discussion of the cause of colitis, which is described as being either of neural or inflammatory origin. In connection with this we are given the report of a patient who had colitis with "tobacco toxis" simulating abdominal aneurism. The most interesting point in his history seems to be that he was about to effect a separation from his wife on account of her bad temper. We then unexpectedly find a section on the influence of colitis on blood-pressure and the intestinal origin of arteriosclerosis, from which we learn that sclerosis and hypertrophied heart are often early results of colitis. This illuminating sentence must be noted: "Chronic intestinal catarrh gives rise to tachycardia in women until Graves' disease is replaced by myxœdema." After this it is pleasing to find some reference to two of our colleagues: "A much more valuable contribution to our knowledge of this most important subject, reaches us from the bank of the Chesapeake in far-off Maryland. No fewer than four thousand cases, many of them drawn from Osler's Clinic at the Johns Hopkins Hospital at Baltimore, have been 'boiled-down' by our indefatigable Transatlantic Brethren; and the resultant Extract of Pathological Pabulum, is of great suggestiveness: it is 'Meat,' indeed." In the opinion of Drs. Thayer and Brush, the "Chefs de Cuisine," the leading Etiological factors are:—

a. Physical Labour, sustained and violent.
b. Alcohol.

As to the acute diseases which predispose to Arteritis:

a. Rheumatic Fever takes the premier position.
b. Enteric Fever comes next, and
c. Malaria—stands third.

The author then points out that enteric fever—second on the list—is a "specialized form of colitis." To consider typhoid fever as a form of mucous colitis is a weird idea.

Then follow descriptions of gastric crises, dilated stomach, displaced kidney, floating kidney, hæmaturia, false floating kidney, orthostatic albuminuria from movable kidney, all of which, while undoubtedly interesting, hardly seem to be applicable in the present volume. Then come sections on elimination, infantilism, and the record of a case of "colitic infantism" in which, after an account of the patient's condition, we learn that he has done well at the university and has now to shave three times a week. Then follows a section on the physical characters of mucus and the description of some of the symptoms of mucous colitis, in which we find the note of a case in which the pain of pleurisy had been treated as a colic. This is no doubt an important observation but its bearing on the subject does not seem evident. The association of colitis with a number of diseases is referred to, but there is nothing of special moment brought out except that the author tends to lay great stress on its association with gout.

Next follows a chapter on "idiopathic colitis or dysentery." It is sad to learn from this that those of us who consider that amœbæ and certain organisms are etiological factors in dysentery are entirely wrong. There are many sections which it is absolutely impossible to review, among them being a discussion of typhus fever. The association of this with colitis we fail to see. Enough has been given to show the general character of the work. The latter part of the book is as much a jumble as the first. Altogether it is a most remarkable book. That it sheds any light on the subject of which it treats is doubtful. That it will furnish amusement to whoever takes the time to read it requires only the proof of a few minutes' perusal. We fear that the complaints from many sources which were the reason for the writing of the book will not be stilled by this response.

Report on the Origin and Spread of Typhoid Fever in the U. S. Military Camps during the Spanish War of 1898. By WALTER REED, Major and Surgeon, U. S. Army, VICTOR C. VAUGHAN, Major and Division Surgeon, U. S. Volunteers, and EDWARD O. SHAKESPEARE, Major and Brigade Surgeon, U. S. Volunteers. Two volumes. (*Washington: Government Printing Office. 1904.*)

It would be remembered that an abstract of this report was published in 1900. We now have it in detail. Of the value of this work it is difficult to speak too highly. It is worthy to take a place with the Medical and Surgical History of the War of the Rebellion. The commission was composed of Major Shakespeare, Major Reed, and Dr. Vaughan of Ann Arbor. Unfortunately, the first two died before the report was completed, so that it had to be finished by Dr. Vaughan. In the letter of transmittal he pays a deserved tribute to the memory of his colleagues. From it we learn that Major Shakespeare worked especially on the question of the dissemination of typhoid fever, and the carefulness of the work in this report is a monument to his industry and zeal. To Major Reed fell especially all matters concerned with the application of sanitary measures.

The report is transmitted in two volumes, the first containing the detailed reports and the second the maps and charts. When one goes over the careful study of the sickness in each regiment and company one realizes what a tremendous amount of work has been done. The tables and summaries are very clearly gotten up and add greatly to the value of the work.

Many of the lessons to be learned from this report have been commented upon previously. As regards the spread of the disease the most important point established is the frequency of direct infection under such conditions as we have when large bodies of troops are collected together, and with this the importance of proper disinfection of the excretions as a preventive. Another fact brought out was the sad lack of ability to recognize typhoid fever in the surgeons who had charge of the troops. This was probably not so much their fault as that of the methods under which they had received instruction.

Some of the more important conclusions of the commission may be quoted:—

1. During the Spanish war of 1898 every regiment constituting the First, Second, Third, Fourth, Fifth, and Seventh Army Corps developed typhoid fever.

2. More than 90 per cent of the volunteer regiments developed typhoid fever within eight weeks after going into camp.

5. Typhoid fever became epidemic in camps located in the Northern as well as those located in the Southern States.

6. Typhoid fever is so widely distributed in this country that one or more cases are likely to appear in any regiment within eight weeks after assembly.

10. These investigations confirm the doctrine of the specific origin of typhoid fever.

11. With typhoid fever as widely disseminated as it is in this country, the chances are that if a regiment of 1300 men should be assembled in any section and kept in a camp the sanitary conditions of which were perfect, one or more cases of typhoid fever would develop.

13. Typhoid fever is more likely to become epidemic in camps than in civil life because of the greater difficulty of disposing of the excretions from the human body.

15. Camp pollution was the greatest sin committed by the troops in 1898.

20. Superior line officers cannot be held blameless for the unsanitary condition of the camps.

21. Greater authority should be given medical officers in questions relating to the hygiene of camps.

22. It may be stated in a general way that the number of cases of typhoid fever in the different camps varied with the methods of disposing of the excretions.

24. The regulation pit system is not a satisfactory method of disposing of fecal matter in permanent camps.

25. In permanent camps, where water carriage cannot be secured, all fecal matter should be disinfected and then carted away from the camp.

26. Infected water was not an important factor in the spread of typhoid fever in the national encampments in 1898.

28. Flies undoubtedly served as carriers of the infection.

29. It is more than likely that men transported infected material on their persons or in their clothing and thus disseminated the disease.

31. It is probable that the infection was disseminated to some extent through the air in the form of dust.

33. When a command badly infected with typhoid fever changes its location it carries the specific agent of the disease in the bodies of the men, in their clothing, bedding, and tentage.

41. Malaria was not a prevalent disease among the troops that remained in the United States.

42. The continued fever that prevailed among the soldiers in this country in 1898 was typhoid fever.

45. About one-fifth of the soldiers in the national encampments in the United States in 1898 developed typhoid fever.

46. Army surgeons correctly diagnosed about half the cases of typhoid fever.

47. The percentage of deaths among typhoid fever cases was 7.61.

Altogether we regard this as one of the most important studies of typhoid fever that has ever been made, and would recommend its careful study to all who are in any way concerned in dealing with the disease. That our knowledge of disease is so increased must be regarded as one of the advantages of the war. Neither the report of the sanitary work in the South African nor the Spanish-American War is pleasant reading for one who believes in the supremacy of the Anglo-Saxon race, but we may hope that the lessons have been laid to heart.

Operative Surgery. By JOSEPH D. BRYANT, M. D., Professor of the Principles and Practice of Surgery, Operative and Clinical Surgery, University and Bellevue Hospital Medical College; Visiting Surgeon to Bellevue and St. Vincent's Hospitals, etc. Two volumes. Fourth edition. Entirely revised and largely re-written. (*New York and London: D. Appleton & Co., 1905.*)

Volume I treats of general principles, anæsthetics, antiseptics, control of hæmorrhage and shock; treatment of operation-wounds and ligatures of arteries; operations on veins, capillaries, nervous system, tendons, ligaments, fasciæ, muscles, bursæ, and bones; amputations and deformities; plastic surgery; operations on the mouth, pharynx, nose, œsophagus, and neck.

Volume II considers operations on the viscera connected with the peritoneum, the scrotum and penis, and miscellaneous operations, including those for some deformities of the external ear.

The first volume is excellent, and with very few exceptions, such as the omission of any mention of injection of the branches of the trifacial nerve with osmic acid for neuralgia, as described by Murphy of Chicago, or of Finney's method of building up the nose, where bones and cartilages have disappeared, by utilization of the phalanges of the left little finger, is up to date and complete.

The second volume covers the ground it undertakes in an equally satisfactory manner, and practically all of the newest operations are taken up and well described.

The illustrations, about 1800 in number and many of them colored, throughout are well chosen, and aid a great deal in explaining the operative methods. Instead of the usual lists of instruments required for different operations, there are photographs of the instruments themselves.

No gynecological operations are considered.

The book is a valuable one, and will be of great use to practical surgeons, and also to practitioners and students who desire to familiarize themselves with modern surgical methods.

Transactions of the American Röntgen Ray Society. (*Philadelphia: A. H. Sickler Company, 1905.*)

This volume contains the transactions of the fifth meeting of the American X-ray Society, held at St. Louis.

The general tone of the articles is much superior to those appearing in the former transactions. There are a number of excellent articles in it, but the most important and interesting is the symposium on malignant disease and the discussions following. Practically every one holds the view that deep-seated and inoperable growths cannot be cured and at best but a temporary checking of the growth with relief of pain may be accomplished.

Carcinoma is purely a surgical disease and should not be given X-ray treatment unless the case is inoperable or the patient cannot undergo an operation. In superficial epitheliomata the results obtained from X-ray treatment are good but, as the symposium points out, we are restricting that class of cases more and more to those where the danger of metastases is not so great.

If the meeting of the American X-ray Society succeeds in impressing this upon the minds of the X-ray operators at large, it will accomplish a great good.

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